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COMPARISON OF EFFECTS OF HORIZONTAL AND
HEAD-DOWN BED REST (NASA) 102 P CSCL 005

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**Joint U.S./U.S.S.R.
Study: Comparison of
Effects of Horizontal and
Head-Down Bed Rest**

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SYMBOLS

ACTH	adrenocorticotrophic hormone	IVCT	isometric ventricular contraction time
ADH	antidiuretic hormone	KS	17-kerosteroids
ALT	alanine aminotransferase	LBNP	lower-body negative pressure
AST	aspartate aminotransferase	LDH	lactic dehydrogenase
BD	body density, g/ml	LVET	left ventricular ejection time
BSA	body surface area	MDH	malate dehydrogenase
BTPS	standard barometric pressure and temperature	MVR	maximum ventilatory rate
BUN	blood urea nitrogen	NS	nonsignificant
CA	catecholamine	OHCS	hydroxycorticosteroid
cAMP	cyclic adenosine monophosphate	25-OHD ₃	25-hydroxycholecalciferol
cGMP	cyclic guanylate monophosphate	PEP	pre-ejection period
ChE	cholinesterase	PP	pulse pressure
CHIBIS	Soviet equivalent for lower-body negative pressure suit	PTH	parathyroid hormone
CO	cardiac output	RER	respiratory exchange ratio
CPK	creatine phosphokinase	RV	residual lung volume, liters
D	density of water	SBP	systolic blood pressure
DBH	dopamine beta-hydroxylase	SDH	sorbital dehydrogenase
DPB	diastolic blood pressure	STH	somatotropin
ECG	electrocardiogram	STI	systolic time interval
EDV	end diastolic volume	SV	stroke volume
EF	ejection fraction	TSH	thyroxine stimulating hormone
ESA	erythroid stimulating activity	T ₃ ,T ₄	thyroxine
ESV	end systolic volume	VCF	velocity of circumferential fiber
HR	heart rate	VCG	vectorcardiogram
HGH	human growth hormone	VCO ₂	carbon dioxide production
GDH	glutamate dehydrogenase	V _E	ventilatory volume
GGTP	glutamate transpeptidase	VO ₂ max	maximal oxygen uptake, ml/kg/min
ICDH	isocitrate dehydrogenase	W _a	body weight in air, kg
		W _w	body weight in water, kg

PREFACE

This report represents the compilation of results for a pioneering effort accomplished by two teams of investigators from the United States and the Soviet Union while participating in the first joint U.S./U.S.S.R. bed-rest study in 1979. In magnitude it compares to the Apollo/Soyuz joint flight test project of 1975 by cooperatively bringing together numbers of Soviets and Americans in a ground-based, medically related effort. Scientifically it allowed for both qualitative and quantitative comparisons of methods and results on human experimentation which continue to bear results for each country.

It is never possible to completely acknowledge and give thanks to all participants in such a large task, which literally numbered in the hundreds of persons. Yet, the project could never have been accomplished without the support of Dr. David Winter, then director of Life Sciences for NASA, Washington, DC, and his replacement Dr. Gerald Soffen, and Dr. Oleg Gazenko, their then Soviet counterpart at the Institute of Medical and Biological Problems (IMBP) in Moscow. Drs. Arnauld Nicogossian, NASA Headquarters; Richard Johnston, Lyndon B. Johnson Space Center (JSC); and Joseph Sharp, Ames Research Center (ARC) provided guidance and the enabling financial and manpower resources on the U.S. side. Final scientific evaluation of the data was accomplished by an editorial team which consisted on the American side of Carolyn S. Leach, Ph.D., Paul Rambaut, D.Sc., and Philip Johnson, M.D. (JSC), and Danielle Goldwater, M.D. (ARC); Leonid I. Kakurin, M.D., Rupert A. Tigranyan, Ph.D., Valerie M. Mikhailov, M.D., and Boris S. Geogievskii, Ph.D., filled the same role for the IMBP. Special thanks is also given to Dee O'Hara, R.N. (ARC), and Andrei N. Nazin, M.D. (IMBP), for their management of respective bed-rest facilities over the course of the studies and to Mrs. Mary Phares for editorial assistance and to Mrs. Doris M. Furman for typing of the manuscript. Specific thanks are also given to particular investigators and their teams: Lester D. Montgomery, Ph.D. (plethysmographic studies), Victor Convertino, Ph.D. (body composition studies and exercise testing), Richard Popp, M.D. (echocardiography), Alvese Polese, M.D. (systolic time intervals, LBNP), Anatoli A. Savilov (echocardiography), Gregori V. Machinskii (LBNP), Galina I. Kozirevskaya (renal studies), and Victor I. Lobachik (radio-isotope studies). Finally, dedication of this work is made in the memory of Dr. Philip Johnson who served as principal U.S. investigator for hematologic studies and Dr. Leonid I. Kakurin, chief project scientist, U.S.S.R. Both have died in the time interval since completion of the study and this report.

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JOINT U.S./U.S.S.R. STUDY:

COMPARISON OF EFFECTS OF HORIZONTAL AND HEAD-DOWN BED REST

SUMMARY

An account is given of results obtained from hypokinesia studies conducted in the Soviet Union (May-June 1979) and the United States (July-August 1979). Both studies were conducted under identical conditions and provided a basis for comparing physiologic reactions and standardizing procedures and methods. Each experiment consisted of three periods: 14 days of pre-bed-rest control, 7 days of bed rest, and a 10- to 14-day recovery period.

Ten male subjects used for both the Soviet and American studies consisted of volunteers with ages ranging from 30-40 years. They were also matched with regard to height, weight, ability to withstand lower body negative pressure (LBNP) and VO_2 max. These groups were subsequently divided into two matched groups of five subjects each, with one group (group "A") subjected to bed rest in a horizontal (0°) body position and the other (group "B") to head-down bed rest (-6°). Daily caloric intake was regulated to 2800-3000 kcal in the control period and 2000-2500 kcal during bed rest, with a return to 2800-3000 kcal during recovery.

Biochemical and hormonal measurements were made of blood and urine, with particular attention given to electrolyte metabolism and kidney function; cardio-pulmonary changes at rest and exercise; influence of LBNP; and incremental exercise using a bicycle ergometer while supine and sitting.

Results of the study allowed us to conclude that a 7-day bed-rest period caused moderate changes to occur in various measured physiologic parameters. Clinical evidence pointed to the fact that head-down bed rest, when compared to the horizontal condition, more closely matched the conditions seen after manned spaceflight. For the most part, statistically significant differences between the two body positions were not observed.

Data from this joint bed-rest study allowed for standardization of baseline conditions for conducting such procedures; established the usefulness of bed-rest procedures for the study of weightlessness; identified those clinico-physiologic parameters most sensitive to change at rest, or with provocation; and provided a means to share future research results, thus reducing duplication by the two countries, through standardization of methods and uniform presentation of results. These investigations also identified a number of new questions applicable for future research projects. The solution to these latter problems

will depend on the possibilities of future joint U.S.S.R. and U.S. studies in the areas of space biology and medicine.

The study was accomplished in two parts: A Soviet part (May to June 1979) and an American part (July to August 1979).

The Soviet experiment was conducted at the Institute of Medical and Biological Problems of the Ministry of Health U.S.S.R. (Moscow) from 14 May to 22 June 1979. The chief scientist for the Soviet experiment was Dr. L. I. Kakurin; the Science Manager was Dr. V. M. Mikhailov. Two American investigator-observers were present at the Soviet experiment, Dr. H. Sandler from Ames Research Center (ARC) (20 May to 14 June 1979) and Dr. C. Alexander from the Lyndon B. Johnson Space Center (28 May to 9 June 1979).

After completion of the first part, agreement was reached that the recovery period after bed rest would be lengthened from 10 days to 14 days and was implemented during the U.S. part of the experiment.

The American experiment was conducted at ARC, Moffett Field, during the period 10 July to 15 August 1979. The chief scientist for the American experiment was Dr. H. Sandler, ARC, and the Science Manager was Dr. C. Alexander, JSC. Two Soviet special observers (Dr. V. M. Mikhailov and Dr. A. I. Grigoriev) were present during this latter test period from 18 July to 5 August 1979.

Results of the Soviet and American experiments were presented by each side at the 10th Joint U.S.S.R. and U.S. Working Group Meeting on Space Biology and Medicine (Houston, TX, October 1979). At that meeting an agreement was also reached for a fuller exchange of information by each side which included individual subject responses for each subject during all tests conducted over the course of the studies. This was transferred to each side as a supplement to the project data at the subsequent 11th Joint Working Group Meeting on Space Biology and Medicine (Moscow, October 1980). A report on the results of the study was jointly prepared by a team of Soviet and American scientists who participated in the study and was presented at the 12th Joint U.S./U.S.S.R. Working Group Meeting on Space Biology and Medicine (Washington, DC, October 1981).

This report represents a summary of the findings given in this final report.

I. INTRODUCTION

Since humans first entered space with the flight of Yuri Gagarin in 1961, U.S. and U.S.S.R. space crews have successfully completed more than 200 missions. In all of these flights, crews have adapted surprisingly well to the weightless environment, with the most notable physiological changes being an unloading of weight bearing; a headward shift of body fluids with resultant facial edema; sensations of blood rushing to the head, and head fullness; and the presence of space motion sickness.

Despite associated symptoms, both astronauts and cosmonauts have consistently been able to perform their assigned tasks in space. However, return to Earth has presented problems, with crews of both space programs time after time exhibiting cardiovascular deconditioning, as evidenced by orthostatic intolerance, loss of exercise capacity, increased heart rates, decreased systolic blood pressure, narrowing of and decrease of pulse pressure, and decreased red cell mass. There has also been significant loss of body weight and muscle mass; instability of gait and coordination; and, in some cases, loss of skeletal mass. These responses have caused considerable concern among aerospace medical personnel of both nations concerning the possibility that prolonged spaceflights may cause health-related problems in participants.

Numerous studies have been conducted using ground-based simulations of weightlessness to seek answers to the mechanisms underlying the observed physiological changes. These have utilized two principal means of simulation: water immersion or bed rest (horizontal and/or head-down). Such studies have been utilized in both countries to uncover mechanisms used by the body to adapt to weightlessness and to test various countermeasures for their subsequent use during spaceflight. Although it is recognized that these procedures do not represent an exact duplication of weightlessness conditions, each model in turn provides distinct changes which mimic conditions regularly seen after actual flight. However, comparisons between ground-based studies conducted between the U.S. and the U.S.S.R. have not been possible because procedures and methods used have not been standardized. By accomplishing this standardization, the data base will be broadened considerably, since it is realized that individual subject differences and time of exposure can markedly influence research results. For example, reported bed-rest studies in the literature have now varied from a few days to a half year or more. Also, different body positions have been reported for bed rest and have varied from horizontal (0°) to -12° or more. Variables measured or tested in a given study have also varied significantly, as have the methods for calculating

and presenting results, even when the same procedure is used.

Therefore, it was proposed that a principal goal for this first Joint Soviet-American study would be a standardization of baseline conditions for the conduct of such ground-based studies, an accurate definition of the best model for use in simulating the early changes occurring with weightlessness, and a listing of those clinico-physiologic parameters most sensitive to change. This was also to include unification of methods for working between the two countries, particularly with regard to techniques and procedures for data handling, calculation, and presentation of results, and the dealing with any other applicable procedures and parameters as various investigators may see fit.

Conducting comparative studies and obtaining solutions to presented problems would allow investigators to obtain primary and derived data and would help in future joint work between the Soviet Union and the United States in the areas of space biology and medicine. In particular overall results would have a significant impact in lowering future costs in conducting bed-rest studies in the two countries by preventing duplication of effort and allowing subsequent exchange of information.

Prior to the present studies, regular contact between biomedical specialists in the U.S. and the U.S.S.R. took place within the framework of the International Federation of Aeronautics, International Academy of Aviation and Space Medicine, Conference Committees on Space Science associated with UNESCO, the "Man in Space" International symposia, and the Joint Working Group on Space Medicine and Biology. These interactions provided the needed contacts to build trust and, finally, the realization of a series of joint medical-biological programs on space medicine and biology which have included animal spaceflight experiments as well as collaboration in human research.

The first important step leading to a cooperative agreement for a joint hypokinesia study took place at the 8th U.S./U.S.S.R. Joint Working Group (Washington, Wallops Island, 1977). The final investigative program was formalized, including the protocol, at the 9th Joint Working Group meeting (Leningrad 11-17 October 1978). The plan consisted of two phases and provided for alternate conduct of an identical study first in the Soviet Union and then the United States. This study stands as a pioneering effort which allowed for the verification of methodology between the U.S. and the U.S.S.R. and future standardization of approaches for such research projects.

Through these studies it was possible to compare the physiological effects of horizontal (0°) and head-down (-6°) body positions as experimental models for weightlessness.

More importantly, the joint project allowed for direct comparison of experimental procedures and methods between the sides, including the manner of data collection and its analysis and presentation. This final report was preceded by preparation and exchange of preliminary data by both sides. This joint venture proved useful and serves as an excellent basis for future cooperative efforts between the U.S.S.R. and the U.S. in the field of Space Medicine and Biology.

II. BACKGROUND

This study utilizes bed-rest techniques that maintain the body in the horizontal and head-down positions as a means of simulating weightlessness.

Both the U.S.S.R. and the U.S. have had a significant number of manned spaceflights which have allowed collection of a large body of information concerning physiological changes under conditions of weightlessness. This information has been collected under medically controlled conditions in flight, and has allowed comparisons of physiologic states before and after flight. These results have shown that weightlessness exposure does result in specific human body adaptations such as (ref. 1):

1. Space motion sickness syndrome (symptoms and signs)
2. Cardiovascular changes, in particular decreases in orthostatic stability and physical work
3. Alteration in fluid/electrolyte balance resulting in decreased circulating blood volume and blood and tissue electrolyte content changes
4. Decreased bone mineral
5. An anemic syndrome manifest by a decrease in red cell mass and thrombocytes and a decrease in red cell lifespan
6. A change in immunological reactivity with a decrease in naturally occurring defense mechanisms

Detailed analysis has shown that the most prominent factor responsible for initiating change was loss of gravity (ref. 2). This is an occurrence unique to spaceflight and must be kept in mind when one gauges the adequacy and experimental usefulness of any model used for its simulation, particularly in assessing mechanisms, magnitude of change, prognostication of crew findings, or evaluation of various countermeasures used during spaceflight.

Medical biological investigations conducted during the Soyuz and Apollo programs and in the Salyut, Mir, and Skylab orbital stations have shown a need for a better understanding of an operant mechanism, particularly for longer-duration exposures and for readaptation following return to Earth (ref. 2).

The single most important occurrence with insertion into orbit is a physical one—the loss of the otherwise normal pull of gravity and a resultant acute absence of normally present hydrostatic pressure columns for the circulation. Blood and body fluid go through a phase of redistribution which is different from conditions on Earth, with increases in flow to organs and parts of the body which are above heart level. This is followed by development of compensatory processes which involve changes in neurohumoral influences and muscle and metabolic processes (refs. 1 and 2). Problems of gravitational redistribution of blood continue to be studied intensively and still pose many unsolved questions regarding their magnitude and need, and means for prevention.

Another important change not usually encountered while on Earth is a loss of muscle activity due not only to the absence of gravity, but to hypokinesia and hypodynamia (ref. 1).

Both of the above weightlessness factors can be studied during ground-based experiments and are the basis for developing various simulation models of weightlessness (ref. 2).

Most work has been devoted to using two experimental models: water immersion and strict bed rest. The rationale for these approaches and their scientific validity have been widely reviewed in both the U.S.S.R. and the U.S. (ref. 2).

Original investigations for modeling long-term weightlessness effects on healthy humans using bed rest started in the Soviet Union and the United States around 1961, the first publications occurring in 1963 (ref. 2). This was followed by many experiments investigating different approaches and exposure durations. These investigations focused on the process of change during the early period of weightlessness and on the evaluation of the effectiveness of different prophylactic drugs.

Analysis of medical data obtained during manned spaceflight has shown that weightlessness changes are variable and are dependent on individual subject reactions (refs. 3 and 4). Nonetheless, the continued need to increase the number of individuals who might participate in a given spaceflight venture and prolonged duration of stay stimulated investigations of drug effects and other countermeasure procedures directed toward supporting higher mental and physical work ability, preventing cardiovascular system problems, and correcting changes in metabolic processes, particularly with regards to fluid/electrolyte and other functional disorders. Changes noted post-flight and following ground-based simulation of weightlessness have demonstrated that ground-based methods can accurately reproduce many weightlessness effects, as well as evaluate different prophylactic drugs and treat disorders. These procedures have returned individual responses to within physiological limits, while

other changes have been observed to remain below a clinical threshold judged to require treatment (ref. 5).

Analysis of previously published material in the Soviet Union and the United States shows that progress has been parallel in the two countries. Nonetheless, there has been a distinct difference in the goals for the studies, with some directed toward answering specific spaceflight-related problems: the Soviet Union accomplishing long-duration spaceflights on the orbital Salyut and Mir space stations, including programs conducted under the sponsorship of Intercosmos; and in the United States for the preparation and accomplishment of manned spaceflights using the Space shuttle. As a result, ground-based studies using bed rest in the Soviet Union have increasingly emphasized the use of longer-duration studies (up to 1 yr) with attention to effectiveness of countermeasures and rehabilitation procedures, while U.S. studies have concentrated on shorter periods (1-2 wk).

There has been interest in both countries regarding untoward physiologic effects during the acute period of adaptation to weightlessness and/or hypokinesia (ref. 1). Information of interest has been gained from selective catheterizations of the heart and great vessels (ref. 6). These studies have provided new information on the cardiovascular effects of body positional change in otherwise healthy individuals. Results have had direct applicability to problems of space, aviation, and clinical medicine.

In the U.S. a large number of bed-rest studies have been conducted in men and women of different ages as a means of uncovering potential problems in their participation in the Space Shuttle program (refs. 1 and 2). Results have shown that bed rest induces a more severe loss in physiological capability in women than in men as manifested in responses to LBNP, +Gz tolerance, and physical work capacity. Most interesting has been the finding that the magnitude of loss does not increase with age in either sex and tends to stabilize in older individuals.

In spite of making significant allowances for the use of horizontal bed rest as a simulator of weightlessness, predictive results from investigations compared to medical investigations in both cosmonauts and astronauts convincingly showed only a fair prognosis. This was particularly the case with regard to postflight orthostatic stability and physical work capacity, deterioration of regulatory posture mechanisms when upright and coordination during walking movements, tone of antigravity muscles and deterioration of metabolic processes, particularly fluid/electrolyte balance. This led to a search for uncovering other approaches and finally to the use of head-down positioning examined under conditions of strict bed rest. This kind of study was started with a 30-day period at a -4° angle (head below the legs) conducted in 1970, and evaluated the effects of prophylactic drugs recommended for the crew of Salyut-1 (ref. 7).

Use of the head-down model has also provided additional information not readily available from the strict horizontal approach and has pointed to changes more closely approximating those reported during actual flight, such as the sensation of increased blood flow to the head, which slowly equilibrated; hyperemia and swelling of the face; instances of illusions where the body seemed to be upside down when the eyes were closed, and so on. Physiological effects were also more pronounced during such ground-based gravity-induced redistribution of blood and paralleled clinically observed data (ref. 8), rheoencephalographic studies (ref. 9), studies of visual and vestibular end-organ responses, and changes of cardiac output (ref. 9), to name a few.

In a 5-day study with subjects bed rested at 0° , -4° , -8° , and -12° , Kakurin and his associates found that the -4° and -8° positions most accurately duplicated heart rate changes with 70° tilt following 5-day spaceflight (ref. 10). Subjective findings have increased with greater head-downward angulation and have consisted of complaints of blood rushing to the head, heaviness of the head, and temporal vessel pulsation, which are similar to complaints by space crews. Objective findings have included neck vein engorgement, increased venous distention of the retinal veins, and increased central and jugular venous pressures. Most of these changes reached maximum intensity within 3 hr of assumption of the head-down position.

Both invasive and noninvasive methods have been used with head-down subjects to study the hemodynamic changes that occur in this position so that results could be compared with those obtained with subjects in the horizontal or upright body position. Mean femoral blood pressure tends to decrease as head-down angulation is increased because of a decrease in both systolic and diastolic blood pressure caused by loss of hydrostatic column lengths, but heart rate (HR) changes very little. Unlike head-up tilt in which central venous, jugular, and left ventricle filling pressures drop significantly, with head-down positioning, central venous pressure increases by about 9 mmHg and jugular pressure increases to more than 30 mmHg. In a 24-hr study with five subjects in the -5° head-down position, Nixon et al. saw a sharp increase in central venous pressure during the first 40 min of bed rest, with a return to baseline values by 90 min, followed by a gradual decline to significantly below baseline by 12 to 16 hr (ref. 11).

In a more recent study by Katkov et al., which placed eight subjects in a -15° head-down position for 7 days, right atrial pressure showed no significant change until the second day, when it began to drop; it continued to drop to the end of the study (ref. 6). At the same time, mean pulmonary artery pressure increased gradually over the first 7 hr and then decreased gradually until the third day. The

difference in changes in right atrial and pulmonary pressure, which are as yet unexplained, raise questions because these changes occurred during the period of bed-rest-induced diuresis. Heart rate, cardiac output (CO), and stroke volume (SV) did not change significantly throughout this latter study.

Echocardiography has not revealed a significant increase in left ventricular end diastolic volume during the first few hours of -5° or -6° head-down bed rest over that measured with horizontal bed rest. In canine studies, Avasthey and Wood, using X-rays of intact dogs, found no increase in heart size when the animals were placed in the -90° position (ref. 12), and Rushmer found that left ventricular dimensions in dogs were greater with animals in the 0° position than with those in either the $+30^{\circ}$ or -30° positions (ref. 13). These findings may have resulted from such factors as a shift of the heart and diaphragm within the chest to accommodate headward fluid shifts and a possible shift in the hydrostatic indifference point for right-heart circulation. Gauer and Thron pointed out originally that this point determines the zero reference level of the low-pressure side of the circulation when the measured pressure shifts from positive to negative (ref. 14). In the supine position, this level occurs at midatrium; in the head-down position, it shifts cephalad to the superior vena cava-atrial junction. These changes help to explain the potential for a decrease in heart size in the head-down position. Nixon et al. did observe some increase in left ventricular dimensions during hourly echocardiographic measurements of subjects in the -5° head-down position, but the changes occurred when central venous pressure had decreased; the cause remains unexplained (ref. 11).

Most hemodynamic changes with head-down bed rest have either paralleled or exceeded findings in the horizontal position, but results have been variable. Kakurin observed exaggerated heart rate responses in head-down subjects during 70° upright tilt (ref. 10). Convertino et al. found that exercise responses following bed rest were more significant with head-down exposure than horizontal (ref. 15). In a 30-day bed-rest study, Katkovskiy and his co-workers saw a greater decrease in exercise capacity following head-down bed rest than in horizontal bed rest (ref. 16). Goldwater et al. found that subjects bed-rested in the head-down position for 7 days exhibited a significantly greater increase in left ventricular and diastolic volume than horizontal subjects, as well as a greater pooling in the legs and pelvis (ref. 17). Hyatt and West, on the other hand, saw no evidence of significant physiological change in eight male subjects bed-rested for 7 days in the horizontal and -5° head-down positions (ref. 18). Neither did Katkov et al. note significant resting hemodynamic changes (HR, CO, and SV) over the course of 7 days of -15° bed rest (ref. 6).

U.S.S.R. investigators have not observed regular increases in resting HR during the first month of head-down bed rest, but have noted significant increases thereafter. Increases in CO during such studies were attributed to increased SV. Changes in CO were usually most prominent by the 6th to 9th day of bed rest and returned to baseline values after 15 to 20 days. Although such changes have occurred in both horizontal and head-down subjects, they occur earlier and are more pronounced in the head-down position. Cardiac output was measured noninvasively in these studies by using CO_2 rebreathing techniques or mechanocardiography; as a result, the findings may be open to question since they differed from those of Katkov et al. who used the indicator dilution method (ref. 6). Changes in blood redistribution with significantly greater headward shift of volume have been documented in the head-down position, with these shifts persisting throughout the bed-rest period. These results were obtained using radioactive iodinated serum albumin and impedance plethysmography, but the quantitative accuracy of these measurements has been questioned (refs. 19 and 20).

U.S.S.R. investigators have used head-down bed rest extensively to test various countermeasures, particularly use of physical exercise, exposure to lower-body negative pressure (LBNP), and electrostimulation of muscles. Before the long-duration flights of U.S.S.R. crews, investigators exposed 18 male subjects to 182 days of -4° head-down bed rest (ref. 21). The subjects were divided into three groups: one group served as controls; a second received daily or weekly exercise regimens; and the third received muscle electrostimulation. Twenty-minute passive stand tests (75° back angle) performed 11 times during the study indicated that the subjects who received exercise and muscle stimulation exhibited fewer presyncope symptoms during testing than the untreated controls. Moreover, systolic time intervals (STI) for the untreated group showed prolonged isometric contractions (pre-ejection period, PEP) and shorter left ventricular ejection time (LVET). Oxygen consumption also was better in the treated subjects. These findings were similar to flight experience in both the Salyut 6 and Skylab missions.

In both the horizontal and head-down positions, bed rest is associated with fluid and electrolyte changes—salt and water diuresis and stimulation of the renin-angiotensin, aldosterone system (ref. 1). Volicer et al. reported that plasma renin activity and plasma aldosterone levels did not differ significantly between horizontal and head-down subjects during the first 6 hr of bed rest, but were significantly increased in head-down subjects (-5°) by the end of 24 hr (ref. 22). In contrast, Nixon et al. reported that plasma renin activity and aldosterone tended to be depressed over the first 12 hr and to return to baseline levels by the end of 24 hr (ref. 11). In this latter study,

blood volume also decreased significantly by 0.6 liters. The difference in these findings is as yet unexplained.

The present study, performed jointly by U.S. and U.S.S.R. investigators, sought to clarify some of the questions concerning horizontal and head-down bed rest.

III. GENERAL PROCEDURES AND METHODS

Subject selection was accomplished in three stages.

Stage 1 (screening) when the subjects were ambulatory included a complete physical examination, including psychological testing, routine hematology and urinalysis, urine tests for renal calculi, SMA-12 (routine blood electrolytes), and blood hormone analysis (24-hr urine and 8-hr blood samples). Subjects were also screened for drug use.

Stage 2 (preliminary) included a 3-hr glucose tolerance test as well as testing for tolerance to exercise (bicycle ergometer) and LBNP.

Stage 3 (final) in which anthropometric data were derived and LBNP tolerance and VO_2 max were compared and subjects were divided into two comparable groups of five persons each.

A total of 60 persons were screened on the Soviet side with 16 individuals subsequently chosen for physiological (Stage 2) testing; 40 individuals volunteered for the American experiment with 20 of these accepted for further evaluation.

The studies consisted of a 14-day control period, 7 days of bed rest, and 14 days of recovery, as shown in figure 1. During the bed-rest segment, five subjects were bed rested in the horizontal position (0°) and five in the head-down (-6°) position.

The U.S.S.R. study was conducted at the Institute for Medical and Biological Problems of the Soviet Ministry of Public Health from May 14 to June 22, 1979; the U.S. study was conducted at the Human Research Facility of NASA Ames Research Center from July 11 to August 15, 1979. Each study was observed by members of the other team.

The subjects selected (ages 31-40 yr) ranged in height from 159 to 185 cm and in weight from 55 to 87.5 kg. Anthropometric data for the subjects are shown in table 1 for the U.S. subjects and in table 2 for the U.S.S.R. subjects; tables 3 and 4 provide cardiovascular baseline data for the two groups, respectively.

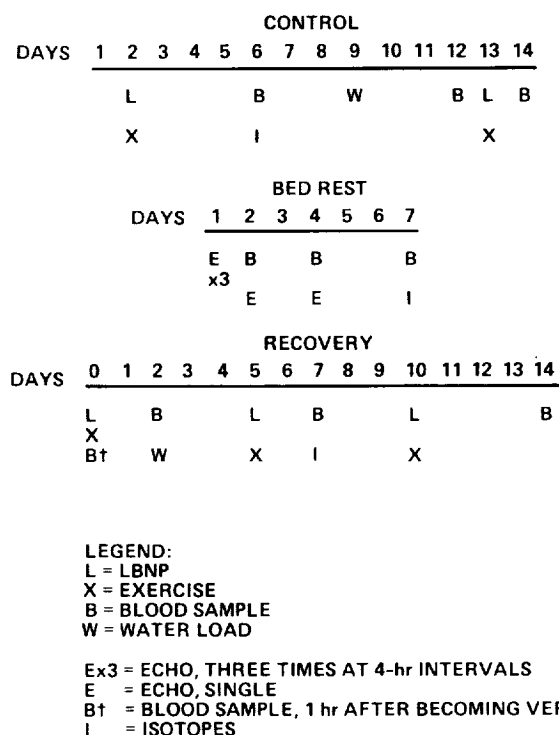


Figure 1.— Study schedule.

All subjects were maintained in facilities providing controlled temperature, noise, and access. The subjects were fed the diets consumed by their national space crews—the Shuttle diet for the U.S. subjects (table 5) and the Salyut orbital station diet for the U.S.S.R. subjects (table 6). Three or four meals a day were provided: breakfast, lunch, dinner, and a late snack, which was optional. The foods were evaluated for content of protein, carbohydrates, fat, sodium, potassium, magnesium, and calcium. The menus were rotated every 4 days in the U.S. study and every 3 days in the U.S.S.R. study. Table 7 compares nutritional values for the two studies. The mean caloric intake for U.S. subjects was 2919 kcal; it consisted of 118 g protein, 429 g carbohydrates, and 81.5 g fat. U.S.S.R. subjects ate 2832 kcal, with 112 g protein, 370 g carbohydrates, and 109 g fat. The U.S. diet differed from that used in previous bed-rest studies in that it included a number of foods (banana, pineapple, chocolate, vanilla, and caffeine-containing beverages) that could produce by-products of metabolism that might interfere with urine test chemistries. Diet samples were not analyzed daily for caloric and mineral content, and true balance studies were not performed. Instead, samples taken of food lots before the study were chemically analyzed for caloric content, moisture, protein, carbohydrates, fat, ash, calcium, iron, phosphorus, magnesium, zinc, potassium, sodium, and

TABLE 1.- ANTHROPOMETRIC DATA ON U.S. SUBJECTS

Subjects, by number	Age, yr	Height, cm	Weight, kg
Horizontal			
108	40	175	74.7
111	38	165	55.2
115	39	171	66.0
118	40	171	70.2
119	38	185	68.7
Mean	39	173	67.0
Head-down			
103	40	180	70.3
105	39	159	58.3
106	36	179	75.0
110	36	175	67.3
113	39	179	74.1
Mean	38	174	69.0

TABLE 2.- ANTHROPOMETRIC DATA ON U.S.S.R. SUBJECTS

Subjects, by designation	Age, yr	Height, cm	Weight, kg
Horizontal			
S-ev	40	183	81.5
S-ov	33	170	81.0
P-ov	33	173	74.8
Sh-ov	31	170	72.0
K-ko	32	170	65.0
Mean	34	173.2	74.9
Head-down			
A-ev	30	173	86.5
P-iy	36	174	73.3
T-in	34	176	87.5
Zh-ov	35	172	81.0
L-iy	38	185	83.3
Mean	35	176	82.3

TABLE 3.- BASELINE RESPONSES TO LOWER BODY NEGATIVE PRESSURE AND EXERCISE STRESS: U.S. STUDY

Subjects	LBNP tolerance at -50 mmHg						
	BSA, m ²	Resting heart rate, beats/min	Max heart rate, beats/min	Duration, min	Blood pressure, mmHg	Max VO ₂ , ml/kg/min	Body fat, %
Horizontal							
108	1.89	68	76	11	120/70	44.5	18.9
111	1.59	58	86	15	140/90	44.6	17.1
115	1.76	66	96	15	118/78	37.0	27.0
118	1.81	78	92	15	120/80	28.4	29.2
119	1.90	86	122	15	120/80	40.5	18.9
Mean	1.79	71	94	14	124/80	39.0	22.2
Head-down							
103	1.89	61	64	15	120/80	38.4	26.7
105	1.59	54	56	8	120/70	45.2	16.1
106	1.92	80	108	15	130/70	31.4	21.3
110	1.81	76	100	15	140/90	35.4	29.2
113	1.92	64	90	15	120/82	41.4	17.4
Mean	1.80	67	84	13	126/78	38.4	22.1

TABLE 4.- BASELINE RESPONSES TO LOWER BODY NEGATIVE PRESSURE AND EXERCISE STRESS:
U.S.S.R. STUDY
[LBNP/Tolerance at -50 mmHg]

Subjects	Heart rate, beats/min	Pulse pressure, mmHg	Maximum VO ₂ , ml/kg/min	Work performed, kg·M
Horizontal				
S-ev	68	20	38.5	13,600
S-ov	120	30	34.8	10,500
P-ov	112	30	40.0	10,500
Sh-ov	74	25	42.2	13,600
K-ko	82	20	48.0	13,600
Mean	91.2	25	40.7	12,360
Head-down				
A-ev	80	40	34.9	13,600
P-iy	94	25	46.9	15,300
T-in	87	45	37.2	15,300
Zh-ov	108	20	33.0	13,600
L-iy	97	30	34.2	12,000
Mean	93.2	32	38.3	13,960

TABLE 5.- SHUTTLE-TYPE DIET USED IN U.S. STUDY

Day 1	Day 2	Day 3	Day 4
Breakfast			
Peach slices (T) Scrambled eggs (R) Bran flakes (R) Bread (toast) (NF) Butter and jelly (NF) Cocoa (B) Orange drink (B)	Applesauce (T) Granola (R) Breakfast roll (NF) Bread (toast) (NF) Butter and jelly (NF) Chocolate instant breakfast (B) Orange-grapefruit drink (B)	Dried peaches (IM) Scrambled eggs (R) Cornflakes (R) Bread (toast) (NF) Butter and jelly (NF) Cocoa (B) Orange-pineapple drink (B)	Dried apricots (IM) Granola with blueberries (R) Bread (toast) (NF) Butter and jelly (NF) Vanilla instant breakfast (B) Grapefruit drink (B)
Lunch			
Frankfurters (T) Bread (2 slices) (NF) Bananas (FD) Almond crunch bar (NF) Apple drink (2 servings)(B)	Corned beef (I) Asparagus (R) Bread (2 slices) (NF) Pear halves (T) Peanuts (NF) Lemonade (2 servings) (B)	Ham (T) Cheese spread (T) Bread (2 slices) (NF) Green beans and broccoli (R) Pineapple (T) Shortbread cookies (NF) Cashews (NF) Tea w/lemon and sugar (2 X) (B)	Diced beef and gravy (T) Noodles and chicken (P) Stewed tomatoes (T) Pears (FD) Almonds (NF) Strawberry drink (B)
Dinner			
Shrimp cocktail (R) Beef steak (I) Rice pilaf (R) Broccoli au gratin (R) Fruit cocktail (T) Grape drink (B)	Beef with BBQ sauce (T) Cauliflower w/cheese (R) Green beans w/mushrooms (R) Lemon pudding (T) Cocoa (B)	Cream of mushroom soup (R) Smoked turkey (I) Mixed Italian vegetables (R) Vanilla pudding (T) Strawberries (R) Tropical punch (b)	Tuna (T) Macaroni and cheese (R) Peas w/butter sauce (R) Pecan cookies (NF) Chocolate pudding (T) Lemonade (B)

Notes: Coffee was available with meals, as desired. B = beverage; FD = freeze-dried; I = irradiated; IM = intermediate moisture; NF = natural form; R = rehydratable; T = thermostabilized. Snacks available in all cases consisted of beverage (coffee, punch, and/or milk); toast; cookies; pudding.

TABLE 6.- U.S.S.R. MENU USED IN STUDY

Day 1	Day 2	Day 3
Breakfast		
Steak Borodinskiy bread Coffee with milk "Ledokol" toffee	Veal Borodinskiy bread Coffee with milk "Ledokol" toffee	Ham Moscow rye bread Cocoa with milk "Ledokol" toffee
Lunch		
Curds with apple jam Walnut wafers Plums and cherries	Curds with cranberry jam "Sakharnoye" pastry Fruit stick of apples-plums	Curds with black currant jam Pastry with cheese Prunes
Dinner		
Beet soup Beef tongue galatine Prunes with walnuts Table bread Sweetened apple-cherry juice	Sauerkraut soup Russian cheese Table bread Prunes with walnuts Black currant juice with pulp	"Kharcho" soup Choice sausage Rye bread Plum cake Sweetened cherry juice
Supper		
Sweet and sour meat Honey cake Candied fruit Tea with sugar	Meat and vegetables "Artika" biscuit Plums and cherries Tea with sugar	Pickled mutton "Sakharnoye" cake Fruit stick of apples-plums Tea with sugar

TABLE 7.- COMPARISON OF NUTRITIONAL VALUES OF U.S. AND U.S.S.R. DIETS

	Calories	Protein, g	Carbohydrates, g	Fat, g
U.S. diet				
Day 1	2906	107.6	430.1	84.1
Day 2	3050	117.4	477.3	74.6
Day 3	3043	124.1	432.0	91.3
Day 4	2678	123.0	375.6	76.0
Mean	2919	118.0	428.8	81.5
U.S.S.R. diet				
Day 1	2839	111.3	378.0	105.1
Day 2	2810	112.3	366.3	109.0
Day 3	2846	111.6	367.0	114.0
Mean	2832	111.7	370.4	109.3

TABLE 8.— CONSTITUENTS OF SHUTTLE-TYPE DIET USED IN U.S. STUDY

Constituent	Day 1	Day 2	Day 3	Day 4	Mean
Calories	2906	3050	3043	2678	2919
Protein, g	107.5	117.35	124.05	122.96	117.98
Carbohydrates, g	430.13	477.34	432.00	375.64	428.80
Fat, g	84.06	74.61	91.29	75.99	81.49
Calcium, mg	1088.0	1362.0	1099.0	1565.0	1278.5
Phosphate, mg	1871.0	1801.0	2223.0	2067.0	1990.5
Potassium, mg	3350	3900	4161	4136	3887
Sodium, mg	4373	3673	6865	4353	4816
Iron, mg	28.2	34.1	24.8	49.6	34.18
Magnesium, mg	399	464	435	752	513

iodine according to the analytical methods of the Association of Agricultural Chemists. Variations in food lots were not known. Uneaten portions of food were weighed and their nutrient values estimated. On this basis it was estimated that the mean intakes of calories and minerals for U.S. subjects were as given in table 8. All subjects drank bottled water throughout the study except during water-load testing when they drank distilled water. Mineral intake for the two types of water was adjusted using information provided by the supplier.

Nutrient intake values were analyzed using a two-way analysis of variance, with one factor representing intake of the subjects and the other representing the time phase of the study. Upon completion of this analysis, means of all significant main effects were compared, using the Newman-Kuels method of testing differences between ordered pairs.

The U.S.S.R. bed-rest subjects were fed a diet similar to that provided the cosmonauts on the Salyut space station (table 6). During the control period that preceded the bed rest period and during the recovery period that followed it, the diet consisted of 2800 kcal/day, composed of 111.7 g protein, 109.4 g fat, and 371.1 g carbohydrates (see table 7). During bed rest, the subjects were fed only 2550 kcal/day consisting of 104.4 g protein, 95.1 g fat, and 317.4 g carbohydrates. The three menus consisted of four meals a day and were rotated every fourth day (see table 6). The subjects consumed all the food provided at each meal. Water was permitted ad libitum, but the intake was recorded.

Throughout the studies, all subjects were monitored twice each day for vital signs (heart rate, blood pressure, and oral temperature) and once a day for body weight. Body weight was measured in the upright position during the control and recovery periods, but on a horizontal bed

scale during the bed-rest period. Emunctory functions also were performed in the bed-rest positions.

All subjects lost weight during the study. In the first few hours of bed rest, the horizontal subjects experienced no unpleasant sensations, but the head-down groups experienced sensations of heat, blood rushing to the head and chest, nose stuffiness, difficulty breathing through the nose, and facial puffiness. By the end of 3 days, these sensations disappeared except for the facial puffiness in the head-down subjects, which persisted throughout the bed-rest period. Following bed rest, all subjects suffered from orthostatic intolerance and pains in the back and leg muscles. These symptoms disappeared within 2-3 days for the horizontal subjects and within 3-4 days for the head-down groups. No health problems were noted as a result of the study.

To assess cardiovascular changes, the subjects in the present study were given electrocardiograms (ECGs) and vectorcardiograms (VCGs), both at rest and under stress using LBNP, echocardiography at rest and when stressed, changes in body geometry and leg volume, and STIs. The methods and results are discussed in the following sections; a comparison of U.S. and U.S.S.R. results is given at the end of each chapter.

IV. HEMODYNAMIC STUDIES

Electrophysiology

U.S. study— U.S. investigators recorded 12-lead ECGs and VCGs for both the horizontal and head-down subjects. The measurements were performed 11 times during the study—2 times during the control period, 6 times during the bed-rest period, and 3 times during recovery.

Twelve-lead ECG measurements were performed with a three-channel instrument (Hewlett-Packard Model 1517A) with recordings at paper speeds of 25 mm/sec and 50 mm/sec. Variables measured were heart rate, P-R intervals, duration of the QRS complex, QT interval, maximum voltage of the T-wave in precordial leads, maximum amplitude of precordial R and precordial S, and the magnitude of R in V₅ and S in V₁. These magnitudes were used, respectively, to determine changes in electrical activity of the left and right ventricles. QTc was calculated by the equation:

$$QTc = \frac{QT}{\sqrt{R - R}} \quad (1)$$

Mean ECG values for the U.S. horizontal and head-down subjects are shown in tables 9 and 10. No statistically significant changes were observed in either group using paired or unpaired t-tests throughout the study, nor was there any evidence of changes in the ST segment or conduction abnormalities. Only two abnormal ECG findings were recorded during the entire study. One horizontally bed-rested subject (No. 111) experienced several ectopic beats (supraventricular) during each LBNP session, but investigators felt that the arrhythmia was not caused by the bed-rest experience. One head-down subject (No. 103), on the other hand, exhibited a prominent U wave in leads V₂ and V₃, but the electrical voltage of this wave decreased progressively throughout the bed-rest period and returned to baseline by day 10 of recovery.

Vectorcardiograms were recorded using a system similar to that used in Skylab in-flight studies (Hewlett-Packard Model 1520A). Leads were placed on each leg, at the back of the neck, and at five positions on the chest (right and left midaxillary line, fifth interspace midline on the front and back of the chest, and fifth interspace mid-nipple line). Two- to three-minute recordings were made on analog tape and subsequently replaced for vector loop display; results and calibration voltages were recorded on polaroid film. Orthogonal X, Y, and Z voltages were recorded on strip charts and later used to create oscilloscope presentations: X and Y to form the frontal plane projection, Y and Z to form sagittal plane projections, and X and Z to form horizontal projections. All three loops were registered in each Polaroid recording (frontal top right, horizontal bottom left, and sagittal bottom left). The individual serial tracings taken throughout the study showed no significant changes in P, QRS, or T loops and agreed with the ECG results reported above.

U.S.S.R. study— U.S.S.R. investigators recorded ECGs at rest seven times during the study—three times during the 14-day control period, three times during the 7-day bed-rest segment, and again on the first day of recovery. Recordings were made using a 12-lead, eight-channel ECG (Minograph-81), with horizontal subjects in the 0° position and head-down subjects in the -6° position. Leads were placed using regular clinical procedures: three standard leads (I, II, and III); three limb leads (ayR, ayL, and ayFO); and six thoracic leads (V₁ through V₆). Control and bed-rest recordings showed normal sinus rhythms. Although HR decreased during the bed-rest period, there were no significant changes in the duration of PQ, QRS, or QRST intervals when corrected for corresponding changes in the length of the R-R interval. Absolute values of the QRST interval and QTc did not deviate from normal by more than 0.04 sec and 5%, respectively. A slight decrease was observed in the amplitude of the T-wave in some cases during bed rest. Tables 11 and 12 show the ECG findings. There was no evidence of significant ST depression (in relation to the isoelectric line) or of T-wave deformities. The ECG findings for both the horizontal and head-down subjects also showed no evidence to indicate metabolic disturbance, interference with the myocardial blood supply, or significant differences between time intervals or waveforms. The slight drop in amplitude of the T-wave that was observed in both groups of subjects was attributed to a change in position of the heart within the chest.

Echocardiography at Rest

U.S. study— Echocardiograms were recorded before and after both the Skylab 4 flight and the U.S.S.R. long-term (96, 140, 175, 185, and 211 days) spaceflights. Most data on cardiac functional and structural changes have been obtained from ground-based studies, primarily bed-rest studies. In the present study, both teams sought to characterize changes in cardiac size and function in order to compare such responses in horizontal and head-down subjects. U.S. investigators performed echocardiographic measurements at rest on both groups of subjects twice during the control period (days 2 and 13), four times on the first day of bed rest, and twice during the remainder of the bed-rest period (days 2 and 4), and twice during recovery (days 5 and 10).

TABLE 9.- ELECTROCARDIOGRAPHIC RESPONSES OF HORIZONTAL (0°) SUBJECTS: U.S. STUDY

M ±SE	HR, beats/min	PR, sec	QRS, sec	QT, sec	QTC, sec	T, mV	SMAX, mV	RMAX, mV	R + S, mV	Rv ₁ + Sv ₅ , mV	Sv ₁ + Rv ₅ , mV
Prebed rest											
Day 2	71 ±3.9	0.18 ±0	0.08 ±0	0.37 ±0.01	0.41 ±0.01	0.6 ±0.01	1.7 ±0.4	1.7 ±0.2	3.6 ±0.3	0.9 ±0.3	2.8 ±0.3
Day 13	69 ±2.1	0.17 ±0.01	0.08 ±0	0.37 ±0	0.40 ±0.01	0.6 ±0.1	1.6 ±0.4	1.5 ±0.3	3.4 ±0.3	0.8 ±0.3	2.8 ±0.4
Bed rest											
Day 1, 0800	65 ±1.9	0.17 ±0.01	0.08 ±0	0.38 ±0	0.39 ±0.01	0.8 ±0.2	1.6 ±0.4	1.8 ±0.2	3.6 ±0.4	0.9 ±0.3	3.1 ±0.5
Day 1, 1300	69 ±3.3	0.17 ±0.01	0.08 ±0	0.48 ±0	0.40 ±0.01	0.7 ±0.2	1.7 ±0.3	1.7 ±0.3	3.4 ±0.5	1.0 ±0.3	2.6 ±0.4
Day 1, 1600	63 ±4.5	0.17 ±0.01	0.08 ±0	0.38 ±0.01	0.38 ±0.01	0.6 ±0.1	1.4 ±0.1	1.8 ±0.3	3.1 ±0.4	1.1 ±0.4	2.6 ±0.3
Day 1, 1900	67 ±2.4	0.17 ±0.01	0.08 ±0	0.38 ±0.01	0.40 ±0.01	0.6 ±0.1	1.2 ±0.3	1.9 ±0.3	2.6 ±0.4	0.7 ±0.1	2.4 ±0.2
Day 2	70 ±2.2	0.18 ±0.01	0.09 ±0	0.37 ±0.01	0.39 ±0.01	0.7 ±0.1	1.7 ±0.2	1.8 ±0.3	3.5 ±0.4	0.9 ±0.3	2.6 ±0.3
Day 4	70 ±2.9	0.18 ±0.01	0.08 ±0	0.38 ±0.01	0.40 ±0.01	0.7 ±0.1	1.7 ±0.3	1.8 ±0.3	3.5 ±0.5	1.1 ±0.3	2.9 ±0.4
Postbed rest											
Day R + 0	70 ±2.0	0.17 ±0.01	0.08 ±0	0.37 ±0	0.40 ±0.01	0.7 ±0	1.8 ±0.2	1.7 ±0.3	3.6 ±0.4	0.8 ±0.3	2.7 ±0.3
Day R + 5	69 ±2.1	0.18 ±0.01	0.08 ±0	0.38 ±0	0.40 ±0.01	0.7 ±0.1	1.9 ±0.2	1.8 ±0.3	3.3 ±0.5	0.8 ±0.3	2.6 ±0.3
Day R + 10	72 ±1.8	0.18 ±0	0.08 ±0	0.37 ±0	0.41 ±0.01	0.6 ±0.1	1.3 ±0.3	1.7 ±0.2	3.0 ±0.4	0.9 ±0.3	2.5 ±0.3

TABLE 10.- ELECTROCARDIOGRAPHIC RESPONSES OF HEAD-DOWN (-6°) SUBJECTS: U.S. STUDY

M \pm SE	HR, beats/min	PR, sec	QRS, sec	QT, sec	QTC, sec	T, mV	SMAX, mV	RMAX, mV	R + S, mV	R _{V1} + S _{V5} , mV	S _{V1} + R _{V5} , mV
Prebed rest											
Day 2	66 \pm 4.1	0.15 \pm 0.01	0.09 \pm 0	0.37 \pm 0.01	0.38 \pm 0.01	0.8 \pm 0.1	1.4 \pm 0.2	1.8 \pm 0.2	3.2 \pm 0.3	1.8 \pm 0.7	3.1 \pm 0.3
Day 13	73 \pm 5.4	0.16 \pm 0.01	0.09 \pm 0	0.37 \pm 0.01	0.41 \pm 0.01	0.9 \pm 0.1	1.3 \pm 0.2	1.9 \pm 0.2	3.3 \pm 0.3	1.7 \pm 0.7	3.0 \pm 0.4
Bed rest											
Day 1, 0800	64 \pm 4.2	0.16 \pm 0.01	0.08 \pm 0.01	0.38 \pm 0.01	0.39 \pm 0.01	0.9 \pm 0.1	1.6 \pm 0.3	2.1 \pm 0.2	3.5 \pm 0.4	1.9 \pm 0.7	3.2 \pm 0.4
Day 1, 1300	66 \pm 5.6	0.15 \pm 0.01	0.09 \pm 0	0.38 \pm 0.01	0.39 \pm 0.01	0.9 \pm 0.1	1.6 \pm 0.3	2.0 \pm 0.2	3.1 \pm 0.3	1.6 \pm 0.6	3.1 \pm 0.4
Day 1, 1600	59 \pm 3.6	0.18 \pm 0.01	0.09 \pm 0	0.38 \pm 0.01	0.38 \pm 0.01	1.0 \pm 0.1	1.1 \pm 0.2	2.0 \pm 0.3	3.1 \pm 0.5	1.6 \pm 0.6	2.7 \pm 0.5
Day 1, 1900	64 \pm 4.6	0.17 \pm 0.01	0.08 \pm 0	0.38 \pm 0.01	0.38 \pm 0.01	0.8 \pm 0.1	1.1 \pm 0.2	1.9 \pm 0.3	3.0 \pm 0.2	1.6 \pm 0.6	2.8 \pm 0.3
Day 2	65 \pm 4.8	0.17 \pm 0.01	0.08 \pm 0	0.37 \pm 0.01	0.39 \pm 0.01	0.8 \pm 0.1	1.4 \pm 0.3	1.9 \pm 0.3	3.0 \pm 0.3	1.5 \pm 0.7	2.7 \pm 0.4
Day 4	64 \pm 4.8	0.16 \pm 0.01	0.08 \pm 0	0.37 \pm 0.01	0.38 \pm 0	0.8 \pm 0.1	1.5 \pm 0.3	1.8 \pm 0.2	3.1 \pm 0.3	1.6 \pm 0.7	3.0 \pm 0.4
Postbed rest											
Day R + 0	69 \pm 5.4	0.16 \pm 0.01	0.08 \pm 0	0.37 \pm 0.02	0.39 \pm 0.01	0.7 \pm 0.1	1.5 \pm 0.3	1.9 \pm 0.2	3.3 \pm 0.3	2.6 \pm 0.3	2.9 \pm 0.3
Day R + 5	80 \pm 5.4	0.16 \pm 0.01	0.08 \pm 0	0.36 \pm 0.02	0.39 \pm 0.01	0.6 \pm 0.1	1.5 \pm 0.3	1.7 \pm 0.2	3.1 \pm 0.3	1.6 \pm 0.7	2.8 \pm 0.3
Day R + 10	75 \pm 3.9	0.16 \pm 0.01	0.08 \pm 0	0.37 \pm 0.02	0.41 \pm 0.01	0.6 \pm 0.1	1.5 \pm 0.3	1.7 \pm 0.3	3.0 \pm 0.4	1.5 \pm 0.7	2.9 \pm 0.3

TABLE 11.- ELECTROCARDIOGRAPHIC RESPONSES OF HORIZONTAL (0°) SUBJECTS:
U.S.S.R. STUDY

Variable	Control			Bed rest			Recovery
	C-13	C-14	Avg.	BR-1	BR-2	BR-4	R+0
R-R, sec	1.01	0.91	0.95	0.99	1.16	1.12	1.0
FHC, beats/min	60	66	63	61	52	54	5
PQ, sec	0.18	0.18	0.18	0.19	0.18	0.18	0.1
QRS, sec	0.08	0.08	0.08	0.08	0.08	0.08	0.0
QRSTu, sec	0.39	0.39	0.39	0.40	0.42	0.41	0.4
QRSTg, sec	0.37	0.35	0.36	0.37	0.39	0.39	0.3
QRST, sec	+0.02	+0.04	+0.03	+0.03	+0.03	+0.02	+0.0
SLR, %	38	42	40	40	36	36	37
SLRQ, %	37	38	37	37	34	34	35
SL, %	1	4	3	3	2	2	3
T _I , mV	0.23	0.28	0.26	0.20	0.27	0.20	0.1
T _{II} , mV	0.26	0.28	0.27	0.27	0.31	0.29	0.2
T _{III} , mV	0.04	0.05	0.05	0.10	0.05	0.11	0.0
Tay R, mV	0.23	0.29	0.26	0.24	0.25	0.26	-0.1
Tay L, mV	0.12	0.09	0.11	0.06	0.10	0.08	0.0
Tay F, mV	0.14	0.17	0.16	0.17	0.16	0.16	0.1
Ty ₁ , mV	0.09	0.12	0.11	0.06	0.10	0.10	0.1
Ty ₂ , mV	0.50	0.51	0.51	0.51	0.68	0.60	0.5
Ty ₃ , mV	0.82	0.63	0.73	0.77	0.87	0.89	0.4
Ty ₄ , mV	0.84	0.82	0.83	0.80	0.91	0.80	0.6
Ty ₅ , mV	0.36	0.39	0.37	0.36	0.45	0.38	0.2
Ty ₆ , mV	0.26	0.28	0.27	0.22	0.30	0.26	0.1

Note: C = control; BR = bed rest; R = recovery.

TABLE 12.- ELECTROCARDIOGRAPHIC RESPONSES OF ANTIORTHOSTATIC (-6°) SUBJECTS:
U.S.S.R. STUDY

Variable	Control			Bed rest			Recovery
	C-13	C-14	Avg.	BR-1	BR-2	BR-4	R+10
R-R, sec	0.99	1.01	1.00	1.01	1.08	1.06	1.14
FHC, beats/min	61	60	60	61	56	57	53
PQ, sec	0.16	0.17	0.17	0.17	0.17	0.16	0.17
QRS, sec	0.08	0.08	0.08	0.08	0.08	0.08	0.09
QRSTu, sec	0.41	0.40	0.41	0.39	0.41	0.41	0.41
QRSTg, sec	0.37	0.37	0.37	0.37	0.38	0.38	0.39
QRST, sec	+0.04	+0.03	+0.04	+0.02	+0.03	+0.03	+0.02
SL _r , %	42	39	41	39	38	39	36
SL _{rq} , %	37	36	37	37	35	36	34
SL, %	+5	+3	+4	+2	+3	+3	+2
T _I , mV	0.20	0.20	0.20	0.20	0.20	0.19	0.14
T _{II} , mV	0.22	0.29	0.25	0.26	0.29	0.25	0.18
T _{III} , mV	0.02	0.11	0.07	0.03	0.12	0.10	0.07
Tay R, mV	-0.24	-0.21	-0.23	-0.22	-0.23	-0.23	-0.16
Tay L, mV	0.07	0.04	0.06	0.06	0.05	0.06	0.02
Tay F, mV	0.13	0.20	0.17	0.18	0.18	0.17	0.13
Ty ₁ , mV	0.06	0.06	0.06	0.01	0.07	0.11	0.10
Ty ₂ , mV	0.42	0.32	0.37	0.29	0.33	0.48	0.44
Ty ₃ , mV	0.64	0.59	0.62	0.60	0.66	0.72	0.58
Ty ₄ , mV	0.66	0.70	0.68	0.69	0.78	0.64	0.59
Ty ₅ , mV	0.28	0.33	0.31	0.29	0.38	0.26	0.24
Ty ₆ , mV	0.19	0.28	0.24	0.22	0.28	0.23	0.17

Note: C = control; BR = bed rest; R = recovery.

The instrument used (Smith-Kline Ekosector I) had both M-mode and scanner capabilities. Transducers of either 1.90 or 2.25 MHz were used for the M-mode, with recordings made on ultraviolet paper (Kodak Linagraph 1895) with a recorder (Honeywell Model 1856A Visicorder) at a paper speed of 50 mm/sec with 7-cm calibration marks. Sector scanner results were recorded (Smith-Kline Model UTC-7100) on magnetic tape. Bipolar sternal electrographic leads were used to record all tracings simultaneously to determine the HR and timing of cardiac events. To obtain the most representational echoes of the anterior and posterior left-ventricle walls, all subjects were placed in the right anterior, oblique chest position (rotated 30°-40° around the longitudinal axis of the body to rest on the left side). For each recording, transducers were positioned in the same interspace and chest location (left fourth and fifth intercostal spaces) to ensure acquisition of reliable and reproducible data. The position of the mitral valve was determined first, and the transducer was then moved toward the cardiac apex until acceptable recordings were obtained of the interventricular septum and rear wall of the left ventricle at the level of the mitral valve chordae. This same approach was also used by both teams of investigators when preparing subjects for echocardiography during LBNP.

The following measurements were obtained from the echocardiographic tracings:

1. Left ventricular end diastolic volume (EDV) diameter: distance from the septal to posterior wall endocardium with the peak of the QRS complex.
2. Left ventricular end systolic volume (ESV) diameter: distance from septal to posterior wall endocardium measured at the point of maximal anterior excursion of the left ventricular posterior wall.
3. Left ventricular ejection time (LVET): from the beginning of anterior motion of the posterior wall to the point of maximal anterior displacement.
4. End systolic and end diastolic ventricular volumes: calculated by the Teichholz formula

$$\text{EDV or ESV} = \left(\frac{7.0}{2.4 + D_{(d \text{ or } s)}} \right) D_{(d \text{ or } s)}^3 \quad (2)$$

5. Mean velocity of circumferential fiber shortening (VCF) was calculated by

$$\text{VCF} = \frac{D_d - D_s / \text{LVET}}{D_d} \quad (3)$$

6. Left ventricular stroke volume (SV) was calculated by

$$\text{SV} = \text{EDV} - \text{ESV} \quad (4)$$

7. Ejection fraction (EF) was calculated by

$$\text{EF} = \text{SV} / \text{EDV} \quad (5)$$

8. Cardiac output (CO) was calculated by

$$\text{CO} = \text{SV} \times \text{HR} \quad (6)$$

where HR is heart rate. Mean values were obtained from 5-10 complete cardiac cycles and used for statistical analyses. The results of echocardiography at rest are shown in table 13 for the U.S. horizontal and head-down subjects.

Heart rate: No significant changes in resting HR occurred in either group during echocardiography, and differences between the two sets of subjects were not significant. Average mean HR was 67.5 ± 2.5 for the horizontal group and 65.2 ± 5.9 for the head-down subjects. The maximum reduction occurred in the horizontal group on the first day of bed rest (at 1900) when they exhibited an average value of 58.8 ± 1.1 ; the comparable value for the head-down subjects was 61.2 ± 7.1 . Thereafter, HR increased progressively in both groups throughout the bed-rest period and into recovery.

Mean arterial pressure: Although mean arterial pressure (MAP) did not differ significantly between the two subject groups, values were consistently higher for the head-down subjects during both the bed-rest and recovery periods. The highest MAP value for this group (93.3 ± 3.4) occurred with the first measurement on the first day of bed rest. This reading was significantly higher ($p < 0.05$) than the baseline value (77 ± 3.1) and remained elevated throughout the remainder of bed rest. Mean arterial pressure also increased in the horizontal subjects, but not significantly, with the highest value (86 ± 3.9) occurring on the first day of bed rest. In both groups, values returned to baseline by the fifth day of recovery.

TABLE 13.- DYNAMICS OF ECHOCARDIOGRAPHY AT REST: U.S. STUDY

Parameter			Control ^a		Bed rest ^a						Recovery ^a		
			C-2	C-13	BR-1 0800	BR-1 1300	BR-1 1600	BR-1 1900	BR-2	BR-4	R + 0	R + 5	R + 10
Heart rate, beats/min													
Horizontal	Mean		67.8	67.5	63.3	65.0	64.3	58.8	64.3	64.5	67.0	70.0	72.5
	SD		7.7	3.3	6.5	5.8	8.2	2.2	2.6	2.9	2.5	4.2	3.4
	SE		3.8	1.7	3.3	2.9	4.1	1.1	1.3	1.4	1.2	2.1	1.7
Head-down	Mean		63.0	67.2	62.6	62.0	59.2	61.2	60.4	68.4	68.3	68.0	67.0
	SD		16.0	11.0	10.8	16.3	14.5	15.8	6.8	10.4	9.7	11.1	7.9
	SE		7.4	4.9	4.8	7.3	6.5	7.1	3.1	4.6	4.3	5.3	3.6
Mean arterial pressure, mmHg													
Horizontal	Mean		73.3	77.5	86.0	86.0	85.3	83.8	84.0	78.8	80.1	72.5	76.5
	SD		6.0	13.9	7.8	7.8	10.1	8.9	7.5	8.3	9.3	10.4	4.4
	SE		3.0	7.0	3.9	3.9	5.1	4.5	3.8	4.1	4.6	5.0	2.2
Head-down	Mean		79.0	77.0	93.3	93.0	87.4	87.6	86.0	90.4	85.4	80.0	78.0
	SD		11.4	6.8	7.7	7.9	11.1	11.1	7.1	9.9	9.9	5.2	10.7
	SE		5.1	3.1	3.4	3.5	4.9	5.0	3.2	4.5	4.4	2.3	4.7
End diastolic volume, ml													
Horizontal	Mean		103.3	96.3	108.0	104.0	103.0	99.8	108.8	105.7	97.0	112.8	105.7
	SD		21.3	26.3	19.1	26.8	20.6	27.0	8.1	20.3	29.8	28.0	20.3
	SE		10.7	13.1	9.6	13.4	10.3	13.5	4.0	10.1	14.9	14.0	10.1
Head-down	Mean		116.2	118.6	108.4	106.4	106.7	102.8	97.0	124.2	116.0	124.0	123.0
	SD		4.9	33.1	14.9	19.6	9.5	16.7	14.8	30.4	36.5	29.0	29.6
	SE		2.2	14.8	6.6	8.8	4.2	7.5	6.6	13.6	16.3	13.0	13.2
End systolic volume, ml													
Horizontal	Mean		31.5	29.0	43.5	32.5	33.3	32.0	33.3	36.5	37.0	44.0	38.5
	SD		7.9	10.9	15.5	4.9	5.3	6.7	5.7	3.0	17.8	24.8	9.6
	SE		3.9	5.5	7.7	2.5	2.6	3.3	2.8	1.5	8.8	12.4	4.8
Head-down	Mean		30.2	35.6	37.2	33.0	36.0	34.0	33.0	41.6	40.6	39.4	39.6
	SD		10.8	17.1	13.4	11.8	9.3	12.0	8.9	16.8	24.8	17.6	13.3
	SE		4.8	7.7	6.0	5.3	4.1	5.5	4.0	7.5	11.1	7.8	5.9

TABLE 13.- CONCLUDED

Parameter	Control ^a		Bed rest ^a						Recovery ^a		
	C-2	C-13	BR-1 0800	BR-1 1300	BR-1 1600	BR-1 1900	BR-2	BR-4	R + 0	R + 5	R + 10
Stroke volume, ml Horizontal	Mean	72.0	67.3	64.5	71.0	70.3	68.0	75.8	69.3	59.0	67.2
	SD	19.6	16.8	8.8	20.9	16.1	23.3	5.9	17.9	14.2	16.0
	SE	9.8	8.4	4.4	10.5	8.1	11.6	2.9	8.9	7.1	8.0
Head-down	Mean	85.6	83.4	70.8	73.0	70.6	68.4	63.4	82.4	75.4	83.6
	SD	8.4	18.2	4.7	10.5	6.2	11.5	10.7	15.3	13.5	16.6
	SE	3.8	8.2	2.1	4.7	2.8	5.2	4.8	6.8	6.0	7.4
Cardiac output, ml/min Horizontal	Mean	4842	4618	4105	4589	4451	4010	4874 ^a	4452	4017	4847
	SD	1249	1151	848	1290	863	1363	471.3	1126	816	1010
	SE	625	576	424	645	432	681	235.1	563	408	505
Head-down	Mean	5435	5493	4436	4559	4165	4251	3833 ^a	5568	4935	5646
	SD	1696	793	833	1422	979	1602	716.5	891	728	1516
	SE	758	354	373	636	438	716	320.5	398	326	678
Ejection fraction, % Horizontal	Mean	0.69	0.70	0.60	0.68	0.68	0.67	0.69	0.65	0.62	0.63
	SD	0.07	0.05	0.08	0.04	0.04	0.08	0.04	0.05	0.08	0.07
	SE	0.04	0.02	0.04	0.02	0.02	0.04	0.02	0.03	0.04	0.04
Head-down	Mean	0.74	0.71	0.67	0.70	0.66	0.67	0.65	0.67	0.67	0.68
	SD	0.08	0.06	0.08	0.06	0.06	0.08	0.06	0.05	0.09	0.04
	SE	0.04	0.03	0.04	0.03	0.03	0.04	0.03	0.02	0.04	0.02
Velocity of circumferential fiber shortening, circ/sec Horizontal	Mean	1.74	1.78	1.46	1.56	1.51	1.56	1.75	1.53	1.51	1.53
	SD	0.23	0.34	0.19	0.20	0.21	0.28	0.14	0.15	0.31	0.30
	SE	0.11	0.17	0.10	0.10	0.6	0.14	0.07	0.07	0.15	0.15
Head-down	Mean	1.82	1.79	1.58	1.74	1.58	1.65	1.55	1.70	1.73	1.70
	SD	0.30	0.19	0.25	0.32	0.24	0.37	0.31	0.23	0.29	0.08
	SE	0.13	0.09	0.11	0.14	0.11	0.16	0.14	0.10	0.13	0.04

^aLetter-number combinations identify test period (e.g., C = control) and day of period. The time is also indicated for bed-rest day 1.

End diastolic volume: Baseline values of EDV were not significantly different between the two groups, although they tended to be slightly higher in the head-down subjects than in the horizontal subjects (118.6 ± 14.8 ml and 96.3 ± 13.1 ml, respectively). Values for the two groups were similar on the first day of bed rest (108 ± 9.6 ml versus 108 ± 6.6 ml), but decreased progressively until 1900 (99.8 ± 13.5 ml for the horizontal subjects and 102.8 ± 7.5 ml for the head-down). On day 2 of bed rest, EDV declined further in the head-down group (97.6 ± 6.6 ml) and increased slightly in the horizontal subjects (108.8 ± 4.0 ml), which created a significant difference between the two groups ($p < 0.05$). These trends were reversed on day 4 of bed rest when four of the five head-down subjects showed an increase in EDV (124.2 ± 13.6 ml) whereas the horizontal subjects showed a slight decrease (105.7 ± 10.1 ml), but the difference between the two was not significant. Throughout the remainder of the bed-rest period, the head-down subjects consistently exhibited a higher EDV. By day 5 of recovery, however, both groups showed signs of returning to normal, although the horizontal subjects exhibited a significant increase (from 97 ± 14.9 to 112.8 ± 14 ml; $p < 0.05$).

End systolic volume: End-systolic-volume responses of the horizontal and head-down groups did not differ significantly. On the first days of bed rest, ESV increased in both groups (horizontal to 43.5 ± 7.7 ml; head-down to 37.2 ml), but decreased toward baseline values in both groups by 1300 that day. During the remainder of bed rest, ESV tended to increase slightly, but became significantly higher for the horizontal group ($p < 0.01$) by day 4 of bed rest. It continued to increase during the recovery period and became significantly higher ($p < 0.05$) in the head-down group by the end of the recovery period, relative to baseline values.

Stroke volume: Baseline values of SV tended to be higher in the head-down subjects (85.6 ± 3.8 ml on control-day 2 (C-2) and 83.4 ± 8.2 ml of C-13) than in the horizontal group (72 ± 9.8 and 67.3 ± 8.4 ml, respectively). By 0800 on day 1 of bed rest, this variable had decreased significantly in the head-down group ($p < 0.05$), but the change in the horizontal group was not significant. It was further reduced in the head-down group (to 63.4 ± 4.8 ml), but increased slightly in the horizontal group (to 75.8 ± 2.9 ml). Throughout the remainder of bed rest, resting SV tended to decrease in both groups, but it returned to baseline values by the fifth day of recovery.

Cardiac output: Changes in CO were closely related to stroke-volume changes since HR did not change significantly in either group during the study. Cardiac output values for the horizontal subjects (mean control value = 4730 ± 749 ml/min) did not change significantly throughout the study, with only slight decreases observed

on the first day of bed rest and on the first day of recovery. The head-down group, on the other hand, exhibited a significant progressive decrease during the first 2 days of bed rest ($p < 0.05$) over their base-line values (mean control value = 5462 ± 384 ml/min; decreased to 3833 ± 321 ml/min). By day 4 of bed rest, however, CO had increased significantly in this group ($p < 0.05$; 5568 ± 398 ml/min), but decreased again significantly ($p < 0.05$) by the end of bed rest. From then until day 5 of recovery, both groups showed increases in CO, but the changes were not significant.

Ejection fraction: Both groups exhibited a reduction in EF on day 1 of bed rest, with the head-down group showing a significant decrease ($p < 0.01$) and the horizontal group showing a similar, but not significant, reduction. By 1300 of day 1, EF in both groups had returned to the range of baseline values. Thereafter, the horizontal subjects showed a steady decrease in EF, which was significant by the end of bed rest ($p < 0.05$). After the initial decrease in EF early in the bed-rest period, the head-down group stabilized at a lower value and did not change further. Mean EF values in both groups remained depressed during the recovery period.

Velocity of circumferential fiber shortening: Changes in VCF were similar to those shown for the ejection fraction. During the first measurement on day 1 of bed rest, both groups showed a reduced VCF compared with baseline values, with the head-down subjects showing a significant decrease ($p < 0.05$). Throughout the remainder of bed rest, both groups exhibited wide variations in VCF, which were similar in magnitude to changes observed in SV and CO. By the end of bed rest, both groups showed values of VCF that were lower than baseline values, but the change was significant only in the horizontal group ($p < 0.01$). Values continued to differ between the two groups during the recovery period, but not significantly.

U.S.S.R. study—Echocardiograms at rest were recorded in the U.S.S.R. study two times during the control period (days 13 and 14), three times on the first day of bed rest, two times during the remainder of bed rest (days 2 and 4), and two times during the recovery period (days 0 and 5). M-mode measurements were made using an Echoline-80 C (Picker Company) concurrent with the ECG (bipolar chest levels) and recorded on ultraviolet paper (Kodak 1895). The transducer was placed in the left fourth or fifth intercostal spaces and positioned in a manner identical to that described above for the U.S. study. All studies were performed with subjects in the right anterior oblique chest position (subjects rotated 30° – 40° about the longitudinal axis of the body to rest on the left side). Subjects were maintained in their respective bed-rest positions (0° and -6°) during echo studies. The two investigative teams measured the same echocardiographic

variables, except for the VCF, which was not derived by U.S.S.R. investigators. As in the U.S. study, the same procedure was used by U.S.S.R. investigators for both the resting echocardiograms and during LBNP.

Baseline mean echocardiographic data for both groups of subjects were similar and are given in table 14. One subject in each group demonstrated relatively high control values of EDV and ESV. In the first 4 days of bed rest, the horizontal subjects exhibited decreases in EDV, ESV, and SV of 11%, 6%, and 14%, respectively, with an attendant decrease in CO (24%). Conversely, the head-down group showed increases in these variables of 10%, 19%, and 3%, respectively, with CO reduced by an average of 7%. During the remainder of bed rest, the horizontal subjects demonstrated lower EDV, ESV, and SV than did the head-down group, for which these measured values remained close to baseline levels. By the end of bed rest (day 7), and relative to day 4 of bed rest, both groups showed decreases in EDV and ESV, whereas CO had increased almost to baseline.

The increase in HR, resulting in decreased EDV, ESV, and SV and increased CO on the first day of recovery, could have resulted from psychological stress associated with anticipating the subsequent LBNP test which followed these measurements. The response of the head-down subjects at this time could also be associated with decreased venous return since the subjects had been moved from the head-down to horizontal position shortly before the resting echo measurements. It should be noted, however, that the head-down group was also tested 2-2.5 hr before the positional change in the head-down position and showed responses in EDV, ESV, SV, and CO close to those seen on day 4 of bed rest, indicating that the observed changes had persisted throughout the bed-rest period.

After the head-down subjects were changed to the horizontal position, they exhibited their largest decreases in EDV and ESV, but this was also associated with significant increases in HR resulting in a maintenance of CO. For example, one subject, when moved from the head-down to horizontal position, showed a decrease in SV (93 ml to 78 ml), but because of an increase in HR (48 to 57 beats/min) CO remained unchanged. Similar changes were observed in the horizontal subjects.

All resting echocardiographic variables returned to baseline values in both groups by the fifth day of recovery. No clinically significant changes in heart activity occurred as the result of either horizontal or head-down bed rest, and the changes that were noted were moderate, functional, and reversible. The difference in heart volume changes between the two groups of subjects deserves some comment. It was felt that the slight decreases in

EDV, ESV, SV, and HR during bed rest in the horizontal subjects were adaptive and directed toward maintaining adequate cardiac output. The decreases in heart volumes in these subjects were best explained by a reduction in circulating blood volume. In the head-down group, the tendency toward increases in EDV and ESV was thought to result from the headward shift of body fluids, which is characteristic of head-down bed rest.

The small number of subjects in the study, the limited duration of bed rest, and significant individual variations among subjects made it difficult to reach valid conclusions concerning patterns of heart-volume changes and alterations in myocardial contractile function.

Lower-Body Negative Pressure

A decrease in orthostatic tolerance has been a consistent finding following exposure to weightlessness, bed rest, immersion, and inactivity. To date, crews in Skylab and Soyuz/Salyut missions have been subjected to orthostatic testing (LBNP) during flight, and all of those tested showed altered responses similar to those seen during ground-based studies. Exposure to LBNP at -50 mmHg has been demonstrated to produce changes in HR and blood pressure, following weightlessness or immobilization, similar to those produced by 70° passive tilt. The observed changes are believed to result primarily from a redistribution of the blood from thoracic reservoirs to pools in the pelvis and vasculature of the legs. However, this hypothesis has not been supported by findings from all research studies (refs. 1 and 2).

The LBNP study compared physiological responses of horizontal and head-down subjects to determine whether either of these bed-rest modes would elicit greater responses than the other. Echo ultrasound was used during LBNP testing to measure total CO and changes in left ventricular volumes with orthostatic stress and to seek answers to the role of myocardial factors in observed orthostatic responses to bed rest.

U.S. study—U.S. investigators used a standard LBNP suction box device for orthostatic stress testing. All subjects were placed in the device in the supine position. A vacuum hood covered the lower extremities and was sealed by a rubber diaphragm at the level of the umbilicus. The LBNP procedures consisted of (1) a 5-min resting control period; (2) 2 min at -25 mmHg, 3 min at -35 mmHg, 5 min at -40 mmHg, 5 min at -50 mmHg; and (3) 5 min of resting recovery. LBNP tests were performed on days 2 and 13 of the study control period, the last day of bed rest (day R + 0), and days 5 and 10 of the study recovery period.

TABLE 14.- DYNAMICS OF ECHOCARDIOGRAPHY AT REST: U.S.S.R. STUDY

Parameter	Control ^a		Bed rest ^a					Recovery ^a		
	C-13	C-14	BR-1	BR-1 + 3 hr	BR-1 + 6 hr	BR-1 + 9 hr	BR-2	BR-4	R + 0	R + 5
End diastolic volume, ml	137	135	136	139	128	127	124	121	118	134
	Mean									
	SD	23	27	25	21	21	15	18	17	23
Head-down	10	13	8	10	9	7	10	8	7	10
	Mean									
	SD	135	131	133	141	141	147	146	133	134
End systolic volume, ml	21	10	16	22	25	20	18	20	23	19
	Mean									
	SE	9	5	5	10	11	9	9	10	8
Horizontal	47	46	47	47	46	46	45	44	40	48
	Mean									
	SD	12	11	11	10	9	9	9	8	13
Head-down	5	5	4	4	4	4	4	4	4	6
	Mean									
	SD	49	45	47	57	57	56	56	47	44
Stroke volume, ml	11	4	9	12	10	9	7	9	11	12
	Mean									
	SE	5	2	3	6	5	4	4	5	5
Horizontal	91	89	90	83	82	81	79	77	76	86
	Mean									
	SD	14	18	15	12	13	12	13	12	11
Head-down	6	9	5	6	6	5	7	6	5	5
	Mean									
	SD	85	86	86	84	84	91	89	85	96
Heart rate, beats/min	11	6	9	12	17	11	13	12	13	9
	Mean									
	SE	5	3	3	5	8	4	6	6	7
Horizontal	62	67	64	56	60	59	59	57	69	61
	Mean									
	SD	8	9	8	7	8	8	7	15	8
Head-down	3	5	3	3	3	4	5	3	7	4
	Mean									
	SD	69	63	66	60	64	64	59	68	79
Horizontal	8	13	10	9	8	5	8	10	10	11
	Mean									
	SE	3	7	3	4	3	2	4	5	5

TABLE 14.- CONCLUDED

Parameter		Control ^a		Bed rest ^a						Recovery ^a	
		C-13	C-14	BR-1	BR-1 + 3 hr	BR-1 + 6 hr	BR-1 + 9 hr	BR-2	BR-4	R + 0	R + 5
Cardiac output, liters											
Horizontal	Mean	5.7	6.0	5.8	4.6	5.0	4.8	4.7	4.4	5.4	5.3
	SD	1.3	1.6	1.4	1.1	1.3	1.1	1.3	1.0	1.4	1.2
	SE	0.6	0.8	0.5	0.4	0.6	0.5	0.6	0.5	0.6	0.5
Head-down	Mean	5.9	5.3	5.7	5.0	5.3	5.8	5.3	5.2	5.8	7.0
	SD	1.1	0.8	1.0	0.7	0.6	0.3	1.1	0.9	1.1	0.5
	SE	0.5	0.4	0.3	0.3	0.3	0.2	0.5	0.4	0.5	0.2
Ejection fraction, %											
Horizontal	Mean	66	66	66	64	64	64	64	64	66	65
	SD	5	4	4	4	2	6	5	5	4	4
	SE	2	2	1	1	1	3	2	2	2	2
Head-down	Mean	64	66	65	60	59	62	62	61	65	68
	SD	4	1	3	5	4	2	2	2	3	5
	SE	2	1	1	2	2	1	1	1	1	3

^aLetter-number combinations identify test period (e.g., C = control) and day of period.

During LBNP, the following physiological variables were measured: HR (sternal ECG leads), blood pressure (cuff and ultrasonic sensor), and EDV, ESV, SV, CO, EF, and VCF (all using echo ultrasound). Wide angle (82°), two-dimensional sector scans were also made during LBNP, and the velocity of temporal artery flow was measured both at rest and during LBNP (transcutaneous Doppler ultrasonic flowmeter) to determine cerebral perfusion. Orthostatic tolerance of the subjects was evaluated on the basis of changes in HR, blood pressure, and CO during testing.

The U.S. investigators used unpaired t-tests to assess differences in responses by the horizontal and head-down subjects. The used paired t-tests to evaluate the orthostatic effects of bed rest and recovery on individual subjects. In evaluating their findings, particular attention was paid to differences between responses at peak LBNP stress (-50 mmHg) and in the resting state, to comparing ambulatory control responses with those at the end of bed rest, and to changes seen during the recovery period (days R + 5 and R + 10). The results are given in tables 15 through 18.

Heart rate: Heart rate responses during LBNP did not differ significantly between the horizontal and head-down subjects, as shown in table 15. Before bed rest, average mean HR during LBNP increased by 21 beats/min in both groups, with the change being significant in both (horizontal = +30%; head-down = +31%; $p < 0.01$). After bed rest, both groups exhibited an even greater increase during LBNP (horizontal = +49%; head-down = +51%; $p < 0.01$). Responses during the recovery period were slightly different for the two groups. On day 5 of recovery, the horizontal group exhibited a greater HR response to peak LBNP, which persisted until day 10 (+38%; $p < 0.01$). On day R + 10, one horizontal subject experienced bradycardia (35 beats/min) and vasopressor syncope with peak LBNP. Mean HR increases during this test were greater and more significant ($p < 0.05$) than those seen in the head-down group, probably because of the response of the subject mentioned above.

Systolic blood pressure: Systolic blood pressure (SBP) responses during LBNP are given in table 16. As would be expected, SBP tended to decrease in both subject groups during LBNP and to increase to baseline values when LBNP was stopped. Throughout the bed-rest period, there was little difference in responses between the two groups. During the recovery period, however, on days R + 5 and R + 10, the horizontal subjects exhibited a

significant ($p < 0.05$) decrease in systolic pressure during -40 and -50 mmHg LBNP, with decreases of 8 and 12 mmHg, respectively, compared with decreases of 3 and 7 mmHg, respectively, in the head-down subjects. Again, the difference may have resulted from the response of the subject described above.

Diastolic blood pressure: Diastolic blood pressure (DBP) (table 17) was generally higher in both groups of subjects at every level of LBNP following bed rest. In the recovery period, the horizontal subjects exhibited a significantly greater increase in resting DBP (10.6%, $p < 0.05$) than did the head-down group (+3.3%, $p < 0.05$).

Mean arterial pressure: In general, MAP (DBP + (SBP - DBP)/3) tended to follow the same patterns as diastolic blood pressure, both during LBNP and after bed rest. With release of LBNP, this variable remained higher than the baseline values in both groups, particularly on the last day of bed rest ($p < 0.05$) and on recovery days R + 5 and R + 10 ($p < 0.05$) for the horizontal subjects.

Throughout most of the LBNP test sessions, MAP was lower in the horizontal subjects, except on day R + 10 of the recovery period. However, it was significantly higher ($p < 0.05$) in the head-down group on day 13 of the control period and on day 5 of recovery. On the last day of bed rest, it was consistently higher (although not significantly so) in both groups of subjects during all LBNP phases. Although there appeared to be a tendency toward recovery in both groups on day R + 5, by day R + 10, the horizontal group exhibited higher MAP, especially at -40 mmHg LBNP ($p < 0.05$). The difference between the two groups was significant, both during -40 mmHg ($p < 0.01$) and after release of pressure ($p < 0.05$).

Pulse pressure: As LBNP stress progressed, both subject groups consistently exhibited decreases in pulse pressure (PP, SBP - DBP) as a result of a decrease in systolic blood pressure and compensatory increase in diastolic blood pressure. The decrease in PP with LBNP paralleled a decrease in SV and CO, which occurred with this procedure. With the removal of LBNP, PP continued to remain lower than baseline values. Pulse pressure at rest and during LBNP showed no consistent trend after bed rest in either group when compared with their respective baseline values. However, the two groups differed significantly ($p < 0.05$) in the direction and magnitude of change following bed rest, with the horizontal group showing a decrease in PP (-4%) and the head-down subjects showing an increase (+16%).

TABLE 15.— AVERAGE HEART RATE RESPONSES TO LOWER BODY NEGATIVE PRESSURE IN HORIZONTAL (0°) AND HEAD-DOWN (−6°) SUBJECTS: U.S. STUDY

Group	LBNP period		Heart rate, beats/min					
			Control day			Recovery day		
			2	13	Average	0	5	10
Horizontal	Control	Mean	68.7	68.9	68.8	68.9	67.3	74.0
		SD	7.3	2.4	4.4	2.7	5.2	4.1
		SE	3.3	1.1	2.0	1.2	2.3	1.9
−6° tilt	Control	Mean	65.5	69.3	67.4	66.7	66.8	68.2
		SD	10.3	11.4	10.1	9.6	10.9	10.7
		SE	4.6	5.1	4.5	4.3	4.9	4.8
Horizontal	−25 mmHg	Mean	73.6	76.2	74.9	76.3	75.9	80.6
		SD	7.6	5.3	5.4	2.4	7.7	6.0
		SE	3.4	2.4	2.4	1.1	3.5	2.7
−6° tilt	−25 mmHg	Mean	70.3	75.2	72.7	75.4	72.2	75.5
		SD	12.9	14.9	13.3	14.3	13.4	13.1
		SE	5.8	6.7	6.0	6.4	6.0	5.9
Horizontal	−35 mmHg	Mean	81.7	81.5	81.6	84.9	82.0	88.2
		SD	10.4	5.7	7.0	4.2	9.0	7.2
		SE	4.7	2.5	3.1	1.9	4.0	3.2
−6° tilt	−35 mmHg	Mean	73.7	79.7	76.7	82.1	76.5	78.8
		SD	11.8	15.8	13.1	16.3	14.0	14.2
		SE	5.3	7.1	5.8	7.3	6.2	6.4
Horizontal	−40 mmHg	Mean	83.0	85.4	84.2	92.6	86.3	95.9
		SD	13.2	5.6	8.6	6.1	13.1	8.8
		SE	5.9	2.5	3.8	2.7	5.9	3.9
−6° tilt	−40 mmHg	Mean	79.1	84.4	81.8	89.3	79.9	82.9
		SD	11.5	17.2	13.2	18.1	13.8	16.8
		SE	5.1	7.7	5.9	8.1	6.2	7.5
Horizontal	−50 mmHg	Mean	89.9	91.0	90.4	102.7	93.8	93.8
		SD	13.3	7.4	9.5	6.1	11.4	21.6
		SE	6.0	3.3	4.2	2.7	5.1	9.7
−6° tilt	−50 mmHg	Mean	84.7	92.0	88.4	101.7	87.5	90.2
		SD	15.4	19.0	15.8	23.9	17.2	17.6
		SE	6.9	8.5	7.1	10.7	7.7	7.8
Horizontal	Recovery	Mean	67.6	66.1	66.9	69.0	66.1	71.4
		SD	10.0	4.4	7.0	3.6	6.1	5.8
		SE	4.5	2.0	3.2	1.6	2.7	2.6
−6° tilt	Recovery	Mean	63.0	69.6	66.3	71.1	66.9	67.9
		SD	10.2	11.2	10.0	14.1	11.4	11.1
		SE	4.6	5.0	4.5	6.3	5.1	4.9

TABLE 16.— SYSTOLIC BLOOD PRESSURE RESPONSES TO LOWER BODY NEGATIVE PRESSURE IN HORIZONTAL (0°) AND HEAD-DOWN (−6°) SUBJECTS: U.S. STUDY

Group	LBNP period		Systolic blood pressure, mmHg					
			Control day			Recovery day		
			2	13	Average	0	5	10
Horizontal	Control	Mean	111.5	109.2	110.3	112.1	107.4	108.8
		SD	11.8	9.2	10.4	14.2	12.3	10.7
		SE	5.3	4.1	4.6	6.4	5.5	4.8
−6° tilt	Control	Mean	120.2	120.9	120.5	123.6	119.0	116.7
		SD	16.2	10.8	11.8	17.7	13.6	9.8
		SE	7.2	4.8	5.3	7.9	6.1	4.4
Horizontal	−25 mmHg	Mean	105.4	106.6	106.0	106.8	103.2	105.6
		SD	12.1	8.7	9.7	8.9	10.7	11.6
		SE	5.4	3.9	4.3	4.0	4.8	5.2
−6° tilt	−25 mmHg	Mean	116.9	119.0	118.0	119.2	117.2	112.5
		SD	19.3	11.0	13.2	19.3	13.8	13.9
		SE	8.6	4.9	5.9	8.6	6.2	6.2
Horizontal	−35 mmHg	Mean	105.0	106.3	105.6	106.3	103.0	104.2
		SD	12.2	6.7	9.0	10.8	13.3	8.2
		SE	5.5	3.0	4.0	4.8	6.0	3.7
−6° tilt	−35 mmHg	Mean	115.2	117.6	116.4	120.2	118.6	113.4
		SD	18.6	13.1	13.8	18.8	16.3	14.0
		SE	8.3	5.9	6.2	8.4	7.3	6.3
Horizontal	−40 mmHg	Mean	105.2	105.2	105.2	108.1	99.8	106.5
		SD	12.4	8.7	10.1	10.2	13.2	10.0
		SE	5.5	3.9	4.5	4.6	5.9	4.5
−6° tilt	−40 mmHg	Mean	117.1	115.0	116.1	121.9	117.4	113.1
		SD	19.3	10.0	14.1	21.2	16.7	9.6
		SE	8.6	4.5	6.3	9.5	7.5	4.3
Horizontal	−50 mmHg	Mean	102.3	101.7	102.0	104.9	99.7	97.0
		SD	13.2	7.6	9.8	9.9	14.5	16.7
		SE	5.9	3.4	4.4	4.4	6.5	7.5
−6° tilt	−50 mmHg	Mean	114.3	111.7	113.0	116.4	116.3	109.5
		SD	21.5	12.7	16.4	19.2	16.3	13.1
		SE	9.6	5.7	7.3	8.6	7.3	5.9
Horizontal	Recovery	Mean	111.6	108.6	110.1	115.4	109.0	109.3
		SD	11.1	10.1	10.5	15.5	13.3	9.5
		SE	4.9	4.5	4.7	6.9	6.0	4.3
−6° tilt	Recovery	Mean	121.7	118.5	120.1	124.2	119.5	111.7
		SD	14.1	11.3	11.9	19.9	13.9	14.1
		SE	6.3	5.1	5.3	8.9	6.2	6.3

TABLE 17.— DIASTOLIC BLOOD PRESSURE RESPONSES TO LOWER BODY NEGATIVE PRESSURE IN HORIZONTAL (0°) AND HEAD-DOWN (–6°) SUBJECTS: U.S. STUDY

Group	LBNP period		Diastolic blood pressure, mmHg					
			Control day			Recovery day		
			2	13	Average	0	5	10
Horizontal	Control	Mean	55.3	54.9	55.1	60.9	56.1	60.4
		SD	4.1	5.2	4.2	6.4	6.9	4.4
		SE	1.8	2.3	1.9	2.9	3.1	2.0
–6° tilt	Control	Mean	60.3	61.7	61.0	63.1	60.6	59.8
		SD	7.8	7.1	4.6	6.0	3.5	7.9
		SE	3.5	3.2	2.0	2.7	1.6	3.5
Horizontal	–25 mmHg	Mean	58.0	58.6	58.3	61.4	57.2 ^a	62.2
		SD	4.8	6.7	5.0	5.8	5.3	7.0
		SE	2.2	3.0	2.2	2.6	2.3	3.1
–6° tilt	–25 mmHg	Mean	62.0	63.7	62.8	65.6	64.5 ^a	59.8
		SD	6.9	5.9	4.1	5.9	1.7	8.8
		SE	3.1	2.6	1.8	2.6	0.8	3.9
Horizontal	–35 mmHg	Mean	57.9	56.2 ^a	57.1	61.6	60.4	63.5
		SD	5.2	3.8	4.3	4.9	8.9	6.8
		SE	2.3	1.7	1.9	2.2	4.0	3.0
–6° tilt	–35 mmHg	Mean	63.8	65.6 ^a	64.7	67.9	64.1	63.5
		SD	9.8	8.3	6.3	7.2	2.3	6.6
		SE	4.4	3.7	2.8	3.2	1.0	3.0
Horizontal	–40 mmHg	Mean	59.2	58.9	59.0	64.5	59.7	65.2
		SD	5.4	3.4	4.3	5.4	7.7	8.4
		SE	2.4	1.5	1.9	2.4	3.4	3.7
–6° tilt	–40 mmHg	Mean	64.1	65.8	65.0	70.7	65.5	64.6
		SD	8.5	6.6	6.2	6.9	3.9	6.5
		SE	3.8	3.0	2.8	3.1	1.7	2.9
Horizontal	–50 mmHg	Mean	60.6	59.4	60.0	66.3	61.5	62.7
		SD	6.0	6.0	5.6	7.6	8.1	10.8
		SE	2.7	2.7	2.5	3.4	3.6	4.8
–6° tilt	–50 mmHg	Mean	64.0	66.2	65.1	70.6	66.0	65.9
		SD	9.9	5.6	6.9	8.7	3.8	8.5
		SE	4.4	2.5	3.1	3.9	1.7	3.8
Horizontal	Recovery	Mean	59.7	59.7	59.7	67.3	61.6	66.2
		SD	4.6	5.3	4.9	9.4	8.5	9.0
		SE	2.1	2.4	2.2	4.2	3.8	4.0
–6° tilt	Recovery	Mean	64.2	64.5	64.3	71.0	62.8	63.1
		SD	7.9	5.1	5.9	8.2	5.8	8.2
		SE	3.5	2.3	2.6	3.7	2.6	3.7

^ap < 0.05 change compared to C-2 or R + 0 test.

TABLE 18.—DYNAMICS OF ECHOCARDIOGRAPHY DURING LBNP: U.S. STUDY

Parameter		Control-period day									Recovery-period day								
		C-2			C-13			Average C-2 + C-13			R + 0			R + 5			R + 10		
		Cont.	Peak LBNP, mmHg	Recov.	Cont.	Peak LBNP, mmHg	Recov.	Cont.	Peak LBNP, mmHg	Recov.	Cont.	Peak LBNP, mmHg	Recov.	Cont.	Peak LBNP, mmHg	Recov.	Cont.	Peak LBNP, mmHg	Recov.
End diastolic volume, ml																			
Horizontal	Mean	103.3	59.0	101.7	96.3	61.8	102.0	99.5	65.5	103.5	97.0	58.7	95.5	112.8	57.0	111.0	105.7	63.0	117.0
	SD	21.3	21.2	17.6	26.3	27.5	28.7	5.8	24.6	8.5	29.8	13.3	30.4	28.0	13.0	37.5	20.3	17.2	34.3
	SE	10.7	15.0	8.8	13.1	16.7	16.6	2.9	12.3	4.3	14.9	6.6	15.2	14.0	6.0	18.8	10.1	8.5	17.2
Head-down	Mean	116.2	72.0	126.0	118.6	81.8	110.0	117.4	77.0	118.0	116.0	51.8	116.0	124.0	68.0	122.0	123.0	74.6	127.6
	SD	4.9	21.8	6.5	33.1	23.1	27.4	18.0	16.0	10.7	36.5	35.8	38.2	29.0	37.6	34.0	29.6	20.7	15.6
	SE	2.2	9.8	2.9	14.8	10.4	12.2	8.0	7.2	4.8	16.3	16.0	17.1	13.0	16.8	15.3	13.2	9.3	7.0
End systolic volume, ml																			
Horizontal	Mean	31.5	14.0	29.0	29.0	20.5	33.0	30.8	20.5	31.8	37.0	22.5	38.0	44.0	23.2	44.8	38.5	20.2	42.5
	SD	7.9	0	8.2	10.9	9.9	13.5	3.1	9.8	7.8	17.8	8.6	13.7	24.8	13.0	27.1	9.6	8.6	18.7
	SE	3.9	0	4.1	5.5	4.9	7.8	1.5	4.9	3.9	8.8	4.3	6.9	12.4	6.5	13.5	4.8	4.3	9.3
Head-down	Mean	30.2	18.0	32.2	35.6	21.8	34.4	33.0	20.0	33.6	40.6	19.4	43.0	39.4	24.8	42.8	39.6	27.6	43.6
	SD	10.8	8.1	8.3	17.1	6.2	13.3	13.5	6.3	10.0	24.8	15.4	26.0	17.6	20.1	20.5	13.3	14.5	13.2
	SE	4.8	3.6	3.7	7.7	2.8	5.9	6.0	2.8	4.5	11.1	6.9	11.4	7.8	9.0	9.2	5.9	6.5	5.9
Stroke volume, ml																			
Horizontal	Mean	72.0	45.0	73.0	67.3	41.3	69.0	69.7	45.2	68.0	59.0	37.0	57.3	68.2	34.0	66.2	67.2	43.0	74.8
	SD	19.6	21.2	21.1	16.8	18.5	18.5	6.4	15.9	6.2	14.2	6.7	18.0	15.7	13.4	17.0	16.0	10.2	18.5
	SE	9.8	15.0	10.5	8.4	9.3	10.7	3.2	7.9	3.1	7.1	3.3	9.0	7.9	6.7	8.5	8.0	5.1	9.3
Head-down	Mean	85.6	54.2	94.0	83.4	60.0	77.0	85.0	57.4	85.8	85.4	32.4	73.0	84.6	43.2	79.6	83.6	47.0	83.8
	SD	8.4	22.9	11.7	18.2	19.9	17.8	9.3	16.2	4.9	13.5	21.0	14.2	12.1	19.8	16.0	16.6	6.9	3.6
	SE	3.8	10.2	5.2	8.2	8.9	8.0	4.6	7.2	2.2	6.0	9.4	6.4	5.4	8.8	7.2	7.4	3.1	1.6

TABLE 18.- CONCLUDED

Parameter		Control-period day									Recovery-period day								
		C-2			C-13			Average C-2 + C-13			R + 0			R + 5			R + 10		
		Cont.	Peak LBNP, mmHg	Recov.	Cont.	Peak LBNP, mmHg	Recov.	Cont.	Peak LBNP, mmHg	Recov.	Cont.	Peak LBNP, mmHg	Recov.	Cont.	Peak LBNP, mmHg	Recov.	Cont.	Peak LBNP, mmHg	Recov.
Cardiac output, ml/min																			
Horizontal	Mean	4842	3522	4472	4618	3633	4243	4730	3869	4595	4017	3790	3583	4811	3031	4160	4847	4345	5058
	SD	1249	1449	1449	1151	1734	1298	71	1511	1039	816	481	930	1159	1556	960	1010	818	745
	SE	625	1025	724	576	867	749	36	756	520	408	240	465	580	778	480	505	409	372
Head-down	Mean	5435	4301	5373	5493	5210	4987	5462	4755	5181	4935	2972	4608	5737	3602	4747	5646	3990	5443
	SD	1696	2263	1458	793	1051	634	859	1322	636	728	1141	408	1086	1564	1020	1516	972	1227
	SE	758	1012	652	354	470	284	384	591	284	326	510	182	485	700	456	678	434	549
Ejection fraction, %																			
Horizontal	Mean	0.69	0.74	0.71	0.70	0.66	0.68	0.69	0.69	0.69	0.62	0.62	0.61	0.62	0.60	0.61	0.63	0.69	0.65
	SD	0.07	0.10	0.10	0.05	0.07	0.08	0.03	0.07	0.05	0.08	0.07	0.04	0.14	0.18	0.13	0.07	0.07	0.07
	SE	0.04	0.07	0.05	0.02	0.03	0.05	0.01	0.03	0.02	0.04	0.03	0.02	0.07	0.09	0.07	0.04	0.03	0.03
Head-down	Mean	0.74	0.73	0.74	0.71	0.74	0.70	0.73	0.74	0.73	0.67	0.63	0.65	0.69	0.65	0.66	0.68	0.65	0.66
	SD	0.08	0.16	0.07	0.06	0.08	0.04	0.07	0.12	0.05	0.09	0.08	0.08	0.06	0.09	0.00	0.04	0.09	0.06
	SE	0.04	0.07	0.03	0.03	0.03	0.02	0.03	0.05	0.02	0.04	0.04	0.04	0.02	0.04	0.03	0.02	0.04	0.03
VCF, circ/sec																			
Horizontal	Mean	1.74	2.11	1.84	1.78	1.97	1.53	1.76	1.99	1.73	1.51	1.73	1.45	1.48	1.68	1.46	1.53	2.08	1.67
	SD	0.23	0.65	0.38	0.34	0.47	0.20	0.12	0.47	0.18	0.31	0.38	0.21	0.51	0.77	0.48	0.30	0.30	0.40
	SE	0.11	0.46	0.19	0.17	0.23	0.11	0.06	0.23	0.09	0.15	0.19	0.11	0.26	0.38	0.24	0.15	0.16	0.18
Head-down	Mean	1.82	2.27	1.91	1.79	2.24	1.77	1.79	2.26	1.84	1.73	1.82	1.59	1.73	1.79	1.63	1.70	1.82	1.59
	SD	0.30	0.77	0.40	0.19	0.37	0.13	0.20	0.49	0.17	0.29	0.36	0.20	0.22	0.37	0.21	0.08	0.28	0.14
	SE	0.13	0.35	0.20	0.09	0.17	0.06	0.09	0.22	0.08	0.13	0.16	0.09	0.10	0.16	0.09	0.04	0.13	0.06

End diastolic volume: Mean values of EDV (table 18) did not differ significantly between the horizontal and head-down subjects during the pre-bed-rest control period, with all subjects exhibiting a decrease (–34% to –35%) at –50 mmHg LBNP. Following bed rest (day R + 0), the horizontal subjects showed a decrease in EDV of 38 ml (–37%) at peak LBNP, whereas the head-down group experienced a decrease of 64 ml (–58%; $p < 0.01$), which was significantly greater ($p < 0.05$) than their control period responses. During the recovery period (days 5 and 10), both groups continued to exhibit greater decreases in EDV with LBNP than they had before bed rest.

End systolic volume: No significant differences in mean values of ESV were seen in the two sets of subjects at rest in the control period. When subjected to LBNP during this period, both groups exhibited a 30%–36% decrease (table 18). With peak LBNP after bed rest, however, the horizontal subjects showed a decrease in ESV of 15 ml (30%), and the head-down subjects experienced a decrease of 21 ml (–52%; $p < 0.05$). During peak LBNP on recovery days 5 and 10, the horizontal group exhibited a greater decrease than they had before bed rest, although resting values were higher and resting ejection fractions lower. At the same time, the head-down subjects exhibited lesser decreases in ESV.

Stroke volume: Stroke volume decreased with –50 mmHg LBNP in both groups during the control period (table 18). Average values for the two LBNP tests during that period (days 2 and 13) showed that the head-down subjects had a significantly higher mean value of resting SV (85 ml) than the horizontal group (70 ml). Following bed rest (day R + 0), the head-down group exhibited a significantly greater decrease in SV, with peak LBNP, of 43 ml (–59%; $p < 0.01$) than the horizontal group with a decrease of 22 ml (–36%). During the recovery period, both groups continued to exhibit SV decreases compared to the baseline values. The horizontal group, however, returned more rapidly to the values that were measured before bed rest. With peak LBNP on day 5 of recovery, these subjects showed a decrease in SV of 34 ml (nonsignificant) and the head-down subjects showed a 41-ml decrease ($p < 0.01$). This trend persisted in the head-down subjects to day 10 of recovery, when they exhibited a 37-ml decrease in SV with peak LBNP stress, whereas the horizontal subjects showed a decrease of only 24 ml. At this testing, the horizontal subjects also displayed increased HR, EF, and VCF during peak LBNP and, consequently, maintained CO.

Cardiac output: There was a consistent decrease in CO during peak LBNP in both groups despite LBNP-induced tachycardia, primarily because of marked decreases in EDV and SV resulting from LBNP (table 18). Following bed rest (day R + 0), the head-down

subjects showed a much greater decrease in CO ($p < 0.05$) with peak LBNP than did the horizontal group—decreases of 1963 ml/min and 228 ml/min, respectively. Between day 13 of the control period and the end of bed rest (day R + 0), the head-down group showed a drop in CO with LBNP from 5210 ml/min to 2972 ml/min, but the horizontal subjects showed no significant change (from 3633 ml/min to 3790 ml/min). Thus, there was a significant difference ($p < 0.05$) between the magnitude and direction of changes in the two groups. The observed changes in CO were primarily a result of changes in SV, since HR increased proportionately (by 56% in the horizontal group and 53% in the head-down group).

By day 5 of recovery, the horizontal subjects exhibited a greater decrease in CO with LBNP than was seen between the control period and the end of bed rest, possibly because of a lesser decrease in HR (–17 beats/min on day R + 5 and –38 beats/min on day R + 0). These subjects also had a greater decrease in SV on day R + 5 (–34 ml) than on day R + 0 (–22 ml). The head-down subjects, on the other hand, exhibited no change in CO in response to LBNP, indicating that deconditioning persisted. However, HR responses during peak LBNP were reduced significantly (–17%) on day R + 5 relative to R + 0, while control-to-peak-LBNP changes on day R + 5 were similar to average responses in the pre-bed-rest control period. It is interesting to note that the head-down subjects experienced this reduction in HR even though their peak LBNP COs and SVs were significantly ($p < 0.05$) lower than pre-bed-rest values.

Ejection fraction and VCF: With LBNP testing following bed rest (days R + 0 and R + 5), the horizontal subjects did not show evidence of LBNP-induced changes in EF and VCF. The head-down subjects, on the other hand, did exhibit greater decreases in EF and VCF (see table 18). The head-down subjects showed changes that were less significant following bed rest. Although MAP in the horizontal subjects at –50 mmHg LBNP on day R + 10 was 6 mmHg lower and diastolic blood pressure was 5 mmHg lower than comparable values for the head-down group, the differences between the two groups probably did not account for the difference in EF and VCF responses between them.

U.S.S.R. study—The LBNP equipment used by the U.S.S.R. investigators differed from that used by the U.S. and consisted of pants worn by the subjects which would support an applied vacuum as shown in figure 2. The device, called the CHIBIS suit, was developed for prophylactic purposes during flight. The pants cover the lower half of the body and contain a waist vacuum seal. The trousers are accordion pleated and held in place, during application of negative pressure, by shoulder suspenders and pressure on the soles of the feet of the outstretched legs.

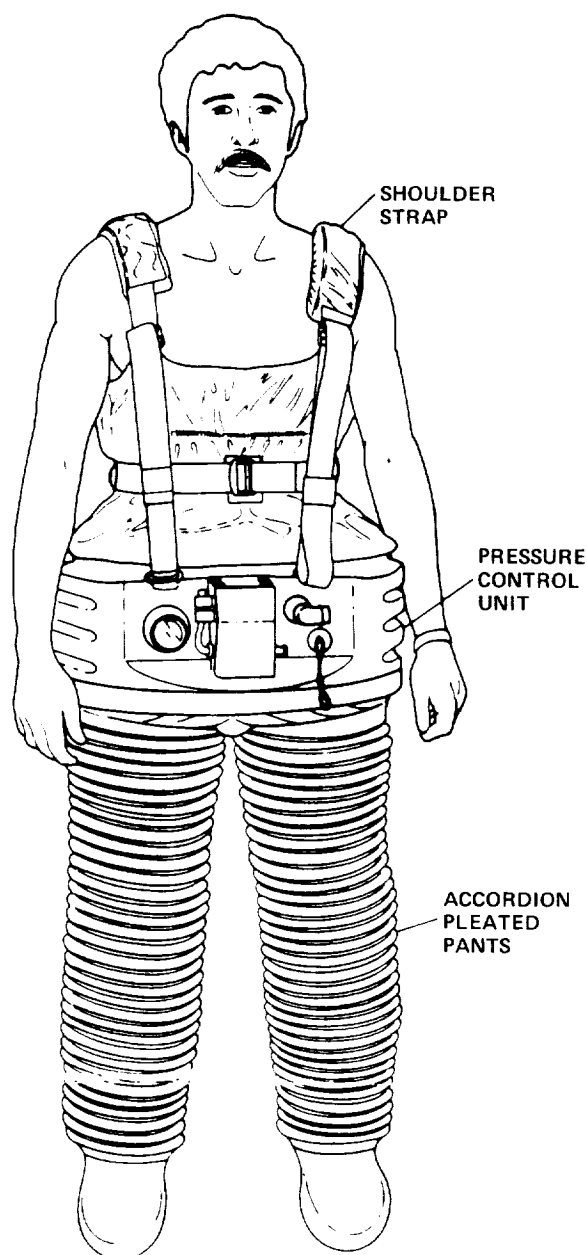


Figure 2.—U.S.S.R. lower-body negative pressure equipment.

All subjects were tested in the supine position and were exposed to the following levels of LBNP: (1) 5 min of resting control; (2) 2 min at -25 mmHg, 3 min at -35 mmHg, 5 min at -40 mmHg, and 5 min at -50 mmHg; and (3) a 5-min recovery period. After the application of peak stress (-50 mmHg), pressure was

returned to atmospheric. The tests were administered at the same time each testing day, twice during the study control period, at the end of bed rest (day R + 0), and on days 5 and 10 of the study recovery period (for one subject, the last test had to be postponed until day 13 because of the subject's toothache). Heart rate and blood pressure changes at peak LBNP before and after bed rest are given in table 19.

During the study control period, all of the horizontal subjects and four of the head-down subjects were able to tolerate LBNP at all levels; one head-down subject, however, was able to tolerate only 4.5 min of -50 mmHg LBNP during the first test in the study control period, but tolerated the second test without difficulty. During LBNP testing, the head-down group exhibited higher HR and lower arterial pressure than the horizontal subjects. However, the differences between the two groups were not significant, as shown in table 19.

Following bed rest, HR and arterial pressure before LBNP were practically identical for the horizontal and head-down subjects, which negated a slight discrepancy between the two observed in the control period. After bed rest, LBNP tolerance decreased in all subjects, and they complained of feelings of weakness, sweating, and dizziness. Frank syncope was not observed on R + 0, but pulse rate increased and arterial pressure decreased to a greater degree than before bed rest. The horizontal subjects demonstrated a significant ($p < 0.01$) decrease in PP, caused primarily by a decrease in systolic arterial pressure during vacuum. Systolic pressure of the horizontal subjects decreased from 121 ± 1.0 mmHg before bed rest to 101 ± 4.0 mmHg afterward, and it decreased from 122 ± 1.0 to 113 ± 4.0 mmHg in the head-down subjects. Changes in diastolic arterial pressure with LBNP were very similar in the two groups, with increases of 12% in the horizontal subjects and 14% in the head-down subjects.

By days 5 and 10 of recovery, LBNP tolerance had improved substantially in most of the subjects. One head-down subject who had been unable to tolerate a full period of -50 mmHg during control-period testing, however, was still unable to tolerate more than 280 sec of -50 mmHg on day 5 of recovery.

U.S.S.R. investigators were able to obtain usable echocardiograms of only four horizontal subjects and three head-down subjects because of subject heart displacements during LBNP, particularly at suction greater than -35 mmHg. The data are given in table 20. Since the number of suitable measurements was so small, the results were not analyzed statistically.

TABLE 19.- HEART RATE, ARTERIAL PRESSURE, AND PULSE PRESSURE WITH LBNP IN HORIZONTAL (0°) AND HEAD-DOWN (-6°) SUBJECTS: U.S.S.R. STUDY

Parameter		Control period			Recovery period								
		Rest	-50 mmHg LBNP Δ	% Δ	R + 0			R + 5			R + 10		
					Rest	-50 mmHg LBNP Δ	% Δ	Rest	-50 mmHg LBNP Δ	% Δ	Rest	-50 mmHg LBNP Δ	% Δ
Heart rate, beats/min													
Horizontal	Mean	65.0	26.0	40	67.0	43.0	66	65.0	26.0	40	69.0	24	35
	SD	12.11	6.7	5.8	14.65	12.3	22	11.13	6.2	7.9	13.22	5.6	13
	SE	5.42	3.04	2.63	6.55	5.59	10	4.98	2.81	3.59	5.91	2.54	6
Head-down	Mean	69.0	29.0	42	68.0	46.0	68	76.0	34.0	45	76.0	27.0	36
	SD	9.06	12.2	18.1	8.44	13.6	16.9	8.86	11.3	17.4	13.33	7.0	1
	SE	4.05	5.54	8.22	3.78	6.18	7.68	3.96	5.13	7.90	5.96	3.18	7
Pulse pressure, mmHg													
Horizontal	Mean	41.0	19.0 ^a	47 ^a	44.0	30.0 ^a	68 ^a	38.0	16.0	41 ^a	42.0	23.0	5.5
	SD	8.94	4.2 ^a	7.9 ^a	4.15	6.6 ^a	11.8 ^a	6.71	6.6	10.6 ^a	6.71	8.4	1
	SE	4.00	1.9 ^a	3.59 ^a	1.86	3.0 ^a	5.36 ^a	3.0	3.0	4.81 ^a	3.0	3.81	6
Head-down	Mean	37.0 ^a	18.0	47 ^a	46.0	20.0	46 ^a	45.0	21.0 ^a	48 ^a	43.0	19.0	44
	SD	5.70 ^a	7.2	17.0 ^a	9.62	7.9	13.9 ^a	11.72	4.2 ^a	9.6 ^a	12.04	6.6	9
	SE	2.55 ^a	3.27	7.72 ^a	4.30	3.59	6.31 ^a	5.24	1.90 ^a	4.36 ^a	5.39	3.0	4
Systolic blood pressure, mmHg													
Horizontal	Mean	127.1	12.7	10	122.4	20.2	16.5	114.4	8.4	7.3	109.2	12.6	11.5
	SD	9.8			3.0			6.0			7.6		
	SE	4.4			1.3			2.7			3.4		
Head-down	Mean	125.7	9.9	7.8	123.2	15.6	12.6	118.2	10.3	8.7	177.2	70.6	39.8
	SD	11.4			13.2			12.7			12.7		
	SE	5.3			5.9			5.7			5.7		
Diastolic blood pressure, mmHg													
Horizontal	Mean	77.5	11.1	14.3	78.0	7.2	9.2	74.0	4.0	5.4	67.6	5.8	8.5
	SD	7.7			5.6			6.1			4.0		
	SE	3.5			2.5			2.7			1.8		
Head-down	Mean	81.6	5.3	6.4	76.1	10.7	14.1	72.4	9.0	12.4	74.6	3.0	4.0
	SD	10.2			11.3			9.1			8.6		
	SE	4.8			5.1			4.2			3.8		

^aSignificant difference from U.S. findings.

TABLE 20.— ECHOCARDIOGRAPHIC DATA DURING LBNP FOR HORIZONTAL (0°) AND ANTIORTHOSTATIC (-6°) SUBJECTS: U.S.S.R. STUDY

Parameter	Group	Control period		Recovery period			
				Day R-0		Day R-5	
		Rest	Peak LBNP	Rest	Peak LBNP	Rest	Peak LBNP
End diastolic volume, ml	0°	138.0	86.0	122.0	71.0	128.0	84.0
	-6°	132.0	95.0	127.0	84.0	133.0	83.0
End systolic volume, ml	0°	46.0	32.0	45.0	33.0	44.0	28.0
	-6°	47.0	38.0	40.0	39.0	43.0	31.0
Stroke volume, ml	0°	92.0	54.0	77.0	38.0	84.0	56.0
	-6°	85.0	57.0	87.0	45.0	90.0	52.0
Heart rate, beats/min	0°	67.0	91.0	67.0	102.0	79.0	104.0
	-6°	66.0	94.0	66.0	112.0	65.0	92.0
Cardiac output, liters/min	0°	6.2	4.9	5.2	3.9	6.6	5.8
	-6°	5.6	5.4	5.7	5.2	5.9	4.8
Ejection fraction, %	0°	67.0	64.0	63.0	54.0	66.0	67.0
	-6°	64.0	60.0	69.0	54.0	68.0	63.0

During the study control period, echocardiography during LBNP showed that HR at peak LBNP increased by 36% in the horizontal subjects and by 42% in the head-down subjects, as shown in table 20. In the horizontal subjects, EDV decreased by 38%, ESV by 31%, and SV by 28%. In the head-down group, EDV decreased by 28%, ESV by 28%, and SV by 43%. Cardiac output also decreased in both groups, but to a greater degree in the head-down subjects (-19.3%) than in the horizontal subjects (-3.4%).

Immediately following bed rest (day R + 0), LBNP responses during echocardiography were intensified in all subjects, particularly HR, which increased by 52% in the horizontal subjects and by 70% in the head-down subjects. In the horizontal group, EDV decreased by 42%, ESV decreased by 27%, and SV decreased by 37%. The head-down group showed decreases of 34% in EDV, 33% in ESV, and 46% in SV. Cardiac output and EF were considerably greater both before and after bed rest in the head-down subjects.

By day 5 of recovery, all variables had returned almost to baseline values, except that the horizontal group exhibited a somewhat greater decrease in CO (-17%) than seen during the control-period testing.

Although fewer in number, the U.S.S.R. echocardiographic findings demonstrated changes similar to those found by the U.S. team in both magnitude and direction.

Left Ventricular Systolic Time Intervals

U.S. investigators recorded left ventricular systolic time intervals (STI) at rest and during LBNP, both before and after bed rest. Measurements of STI made during LBNP were obtained at peak stress (-50 mmHg) and during recovery (release of suction). First and second heart sounds were obtained with a microphone (Elma-Schonander EMT 25) placed over the precordium at the fourth right interspace near the sternum. Carotid pulse was recorded (Sanborn APT/16/1 transducer), and temporal artery pulse was measured with a continuous-wave Doppler velocity system (L&M Directional Ultrasonic Flowmeter Model 1012). Because no difference was found between carotid and temporal artery pulses, LVET was determined from the more technically definitive tracings of the Doppler flowmeter with the value determined from the beginning upstroke of the velocity trace to the trough of the incisura. The interval between the first and second heart sound (S₁S₂) was measured from the

beginning of the first sound to the onset of the aortic component of the second sound. The duration of total electromechanical systole was measured directly from the onset of the Q-wave of the ECG to the beginning of the second heart sound (QS₂). All data were recorded using an eight-channel ink recorder (Gould Brush 200) at a paper speed of 100 mm/sec.

The pre-ejection period was calculated by subtracting LVET from QS₂; the QS₁ interval was calculated by subtracting S₁S₂ from QS₂; and the isovolumnic was calculated by subtracting LVET from S₁S₂. Observed values of QS₂, LVET, and PEP were corrected for HR responses using the following equations developed by Weissler et al. (ref. 22):

$$QS_2' = 2.1 \text{ HR} + QS_2 \quad (7)$$

$$\text{LVET}' = 1.7 \text{ HR} + \text{LVET} \quad (8)$$

$$\text{PEP}' = 0.4 \text{ HR} + \text{PEP} \quad (9)$$

All intervals were calculated from the mean of five consecutive beats, with each beat measured to the closest 5 msec. Results are shown in table 21. Changes within each group were analyzed by using a paired t-test and changes between the two groups were analyzed by using an unpaired t-test.

This noninvasive technique has become widely used for clinically evaluating left ventricular function under a variety of conditions (ref. 23). In several previous investigations, in which the technique was used with bed rest, it was consistently found that LVET is shortened and that the PEP is lengthened, resulting in an increase in PEP/LVET. The mechanisms underlying these changes are not yet understood, but appear to be related to decreased myocardial contractility or to changes in cardiac function, because of decreases in plasma volume regularly seen with immobilization.

However, differences in resting STI measurements between the horizontal and head-down subjects before and after bed rest were not significant. As would be expected, LBNP affected both groups. During control-period measurements with LBNP, the two groups exhibited similar decreases in LVET intervals (horizontal = -40 msec, $p < 0.05$; head-down = -34 msec, $p < 0.05$). PEP intervals and PEP/LVET, on the other hand, increased in both groups, with the horizontal subjects showing increases of +19 msec in PEP intervals ($p < 0.05$) and an increase of +0.19 in PEP/LVET ($p < 0.05$); the head-down subjects showed increases of +20 msec in PEP interval ($p < 0.05$) and +0.18 in PEP/LVET ($p < 0.05$). Values following bed rest did not differ significantly within either group or between the two

groups from control (pre-bed-rest) values. Therefore, there was no evidence of a change in myocardial contractility following bed rest using these methods.

Plethysmography and Body Composition

Many LBNP studies have dealt with the redistribution of blood and fluids during bed rest in attempts to clarify whether such changes are responsible for the cardiovascular deconditioning seen after actual spaceflight and after bed-rest and other ground-based simulations. Despite differences in methods and conditions in the various investigations, the findings have been similar—that is, the volume of the lower leg increases in proportion to the level of suction applied and the volume rate of blood flow to the forearm is decreased. It has also been suggested that orthostatic intolerance following restricted muscular activity is associated with altered blood vessel tone (both arterial and venous) and increased distensibility of the vascular bed of the lower extremities. To date, no conclusive data supporting such hypotheses have been obtained in ground-based studies. Some investigations, in fact, have indicated that prolonged immersion, chair rest, and bed rest do not significantly change the distensibility of the lower extremity vascular bed, but, rather, may even increase the tone of blood vessels (ref. 2). Even less is known about volume changes in subjects bed-rested in the head-down position. Toward this end, impedance and occlusion plethysmography were used to estimate the blood rate and distensibility of extremity vessels for subjects in this study (ref. 24).

U.S. study—Headward shifts of body fluids have been observed consistently during initial exposure to weightlessness, but as yet the physiological consequences of this change have not been explained. U.S. investigators used plethysmography for the following purposes:

1. To determine volume changes that occur in various segments of the body during bed rest
2. To determine the temporal course of such changes
3. To correlate segmental fluid shifts with changes in anthropometric volume that occur during bed rest
4. To compare the redistribution of body fluids that occurs in horizontal and head-down subjects with bed rest

The plethysmography tests were conducted between 1400 and 1600 on days 2, 8, and 14 of the control period; days 1, 4, and 7 of bed rest; and days 0, 8, and 9 of recovery. On the last testing day, an additional test was conducted between 0700 and 0800, before the subjects had risen, to determine whether fluid redistribution occurred during the sleep period. All measurements were made with the subjects in the supine position.

TABLE 21.- SYSTOLIC TIME INTERVALS

	PEP interval, msec						QS ₁ interval, msec					
	Before bed rest			After bed rest			Before bed rest			After bed rest		
	Control ^a	Peak LBNP	Recovery ^a	Control ^a	Peak LBNP	Recovery ^a	Control ^a	Peak LBNP	Recovery ^a	Control ^a	Peak LBNP	Recovery ^a
Horizontal												
Mean	128	147 ^b	138	133	146 ^b	137	67	69	70	51	64	69
SD	7.3	10.9	5.3	9.6	28.1	16	4.4	12.9	6.8	20.2	8.4	30.2
SE	3.3	4.9	2.4	4.4	12.7	7.3	2	5.9	3.1	9.2	3.8	13.7
-6° tilt												
Mean	125	145 ^b	124	132	145 ^b	138	63	58	60	52	56	66
SD	15.2	18.5	15.2	17.6	67.2	18.5	17.6	14.4	18.4	16.8	8.4	33.6
SE	6.9	8.4	6.9	8	30.6	8.4	8	6.6	8.4	7.6	3.8	15.3
	QS ₂ interval, msec						LVET interval, msec					
	Before bed rest			After bed rest			Before bed rest			After bed rest		
	Control ^a	Peak LBNP	Recovery ^a	Control ^a	Peak LBNP	Recovery ^a	Control ^a	Peak LBNP	Recovery ^a	Control ^a	Peak LBNP	Recovery ^a
Horizontal												
Mean	529	510	526	518	523	526	402	362 ^b	389	408	368 ^b	381
SD	7.3	14.4	12.2	20.2	7.8	30.2	13.7	13.7	11.6	65.6	25	10.9
SE	3.3	6.5	5.6	9.2	3.6	13.7	6.2	6.2	5.2	29.8	11.4	4.9
-6° tilt												
Mean	525	510	514	525	510	515	400	366 ^b	390	384	363 ^b	371
SD	16.8	20.2	20.2	16.4	20.2	28.1	9	18.5	7.3	29.2	19.3	24
SE	7.6	9.2	9.2	7.4	9.2	12.7	4.1	8.4	3.3	13.2	8.8	10.9

TABLE 21.– CONCLUDED

	IVCT interval, msec						PEP/LVET interval, msec					
	Before bed rest			After bed rest			Before bed rest			After bed rest		
	Control ^a	Peak LBNP	Recovery ^a	Control ^a	Peak LBNP	Recovery ^a	Control ^a	Peak LBNP	Recovery ^a	Control ^a	Peak LBNP	Recovery ^a
Horizontal												
Mean	33	39	38	35	39	38	0.356	0.546 ^b	0.404	0.394	0.550 ^b	0.410
SD	4.4	12.2	5.8	9.6	3.6	6.2	0.04	0.09	0.16	0.36	0.09	0.09
SE	2	5.6	2.6	4.4	1.6	2.8	0.02	0.04	0.07	0.16	0.04	0.04
-6° tilt												
Mean	35	39	37	33	40	35	0.346	0.524 ^b	0.352	0.400	0.520 ^b	0.430
SD	4.8	7.3	4.4	4.4	11.6	4.8	0.09	0.16	0.01	0.09	0.36	0.04
SE	2.2	3.3	2	2	5.2	2.2	0.04	0.07	0.0	0.04	0.16	0.02

^aQS₁ – time interval from onset of Q-wave to first heart sound.^bDifference from the control value of the same LBNP phase significant at $p < 0.05$.

Baseline resistance of the calf, thigh, total leg, pelvis, torso, and midthigh were measured during each test sequence, using an impedance rheograph (Princeton Applied Research). Disposable ECG electrodes (Hewlett-Packard) were placed in the same position for each test and attached to the foot, ankle, knee, and midthigh (opposite the groin) of each subject's dominant leg; to the wrist and shoulder of the dominant arm; and at the iliac crest on the same side of the body. The ankle, thigh, and midthigh electrodes defined the extent of the calf, thigh, and whole-leg segments. The midthigh and iliac crest electrodes defined the pelvic segment, and the iliac crest and shoulder electrodes defined the torso segment. The wrist and shoulder electrodes defined the arm segment. Whole-body measurements were made from values obtained between the wrist and ankle electrodes, and those for the total leg came from measurements between the ankle and midthigh electrodes.

Before each impedance test, the subject was measured to determine the geometric dimensions of the leg, pelvis, and area between the electrodes defining those segments. Leg and arm circumferences were measured at 3-cm intervals according to the procedure used in the Skylab experiments. Pelvic circumferences were measured at the iliac crest, midthigh position, and midway between the two. The circumferences and lengths of the various segments were then averaged, and the cylindrical volume of each segment was calculated from the results. The segmental length was considered to be the conductive length for each segment, with the whole-body conductive length being the sum of the leg, pelvic, and arm lengths plus the distance between the iliac crest and shoulder electrodes. Segmental geometric volumes were calculated for the calf, thigh, whole-leg, pelvic, and arm segments, but not for the torso and whole-body segments. The results were then correlated with electric impedance volumes calculated from the corresponding R_0 values for each segment.

A two-tailed, paired Student's t-test was used to compare the responses of each subject on the various test days, and a two-tailed Student's t-test for independent data was used to compare findings for horizontal and head-down subjects. A rejection criterion of $p < 0.05$ was used throughout. Resting geometric and electric volume changes for the forearm are shown in table 22; changes for the whole leg are shown in table 23. Segmental electric volumes and whole-body water values were calculated

using the resistivity for blood of 150 ohm-cm. In the recovery period, the horizontal subjects showed an increase in volume in all segments except with testing on recovery day 8 and the first test on day 9 when they lost volume. Aside from these occasions, the day-to-day segmental volume changes in the horizontal group were gradual and not significant, the greatest changes occurring in the ambulatory control period. It should also be noted that the tests on the mornings of recovery days 8 and 9 were separated by 8 hr of ambulation and 8 hr of sleep, which suggests that fluid shifts occurring in the body require 4-6 hr to become significant. Comparison of the results of individual tests, however, showed that the horizontal subjects exhibited a significant decrease ($p < 0.05$) in electric volumes of the lower extremities during the 14-day control period, but did not change significantly in this regard during bed rest.

In the head-down group, segmental electric volumes of the calf and thigh did not change to the degree observed in the horizontal group. Although this group exhibited significant decreases ($p < 0.05$) in these segments during the control period, they remained fairly stable throughout the rest of the study and did not show notable differences on the mornings of recovery days 8 and 9. Changes in whole-leg electric volume in this group were similar to those seen in the horizontal subjects. Electric pelvic volume decreased significantly in the head-down group during the control period, increased significantly on day 4 of bed rest, and again decreased during the last 3 days of bed rest. Electric volume of the arm segment also decreased significantly between control testing and the first 4 days of bed rest. Electric torso volume changes in the head-down subjects were substantially different from those seen in the horizontal group, with the head-down subjects showing a significant decrease between tests on days 8 and 14 of the control period, a significant increase on the first day of bed rest, a slight increase between days 1 and 4 of bed rest, and a significant increase between days 4 and 7 of bed rest.

U.S. investigators also calculated **whole-body water** responses for each subject during the study, using whole-body resistance values according to Bernard et al. (ref. 25):

$$\text{Whole - body water (liters)} = 0.62 \times 10^{-4} \frac{T^{-2}}{R_0} \quad (10)$$

TABLE 22.— VOLUME CHANGES IN THE FOREARM DURING PLETHYSMOGRAPHY AT REST—COMPARISON OF GEOMETRIC AND ELECTRICAL VALUES: U.S. STUDY

		Control-period day			Bed-rest day			Recovery day	
		C-2	C-8	C-14	BR-1	BR-4	BR-7	R + 0	R + 8
		Geometric volume, ml							
Horizontal (N = 5)	Mean	2369.6	2234.3	2297.9	2231.7	2234.7	2279.3	2269.5	2292.6
	SD	288.4	204.7	315.6	304.9	311.0	299.1	276.5	296.7
	SE	218.9	91.5	141.2	136.4	139.1	133.8	123.6	132.7
Head-down (N = 5)	Mean	2415.6	2441.5	2440.3	2407.3	2396.5	2406.6	2299.9	2353.9
	SD	514.2	408.8	396.9	412.6	561.9	449.6	467.3	512.3
	SE	230.0	182.8	177.5	184.5	251.3	201.1	209.0	229.1
		Electrical volume, ml							
Horizontal (N = 5)	Mean	1718.9	1481.4	1491.4	1458.2	1459.3	1437.1	1448.9	1503.9
	SD	228.5	82.3	195.7	205.9	199.6	170.8	127.3	146.2
	SE	102.2	36.8	87.5	92.1	89.3	76.4	56.9	65.4
Head-down (N = 5)	Mean	1709.3	1662.3	1590.6	1553.6	1599.6	1619.9	1361.7	1492.7
	SD	429.9	318.1	328.2	298.8	329.3	435.2	309.6	430.6
	SE	192.3	142.3	146.8	133.6	147.3	194.6	138.5	152.3

Note: Regression equations of comparison: horizontal, $V_g = 1.12 V_e + 603.47$; $r = 0.79$ and $n = 50$; head-down, $V_g = 1.21 V_e + 495.88$; $r = 0.92$ and $n = 50$; combined, $V_g = 1.19 V_e + 510.01$; $r = 0.89$ and $n = 100$.

TABLE 23.— VOLUME CHANGES IN THE WHOLE LEG DURING PLETHYSMOGRAPHY AT REST—COMPARISON OF GEOMETRIC AND ELECTRICAL VALUES: U.S. STUDY

		Control-period day			Bed-rest day			Recovery day	
		C-2	C-8	C-14	BR-1	BR-4	BR-7	R + 0	R + 5
		Geometric volume, ml							
Horizontal (N = 5)	Mean	6984.1	6761.9	6676.7	6374.4	6354.4	6463.6	6605.8	6447.6
	SD	1217.8	930.1	867.9	1169.6	1064.9	1108.5	1213.8	1044.9
	SE	544.6	415.9	388.2	523.1	476.2	495.7	542.8	467.3
Head-down (N = 5)	Mean	7369.0	7550.4	7340.7	7090.4	7101.9	7086.9	7108.7	7152.3
	SD	1526.8	1525.9	1321.9	1378.1	1456.4	1219.3	1396.9	1447.3
	SE	682.8	682.4	591.2	616.3	651.3	545.3	624.7	647.3
		Electrical volume, ml							
Horizontal (N = 5)	Mean	3492.5	3263.0	3056.9	2877.6	2789.8	2783.3	3056.4	3063.0
	SD	312.2	663.8	434.8	509.8	495.4	474.9	616.9	505.8
	SE	139.6	296.9	194.4	227.9	221.6	212.4	275.9	226.2
Head-down (N = 5)	Mean	3728.7	3466.9	3368.8	3067.4	3129.5	3080.1	3170.4	3235.3
	SD	920.8	805.3	708.4	619.9	833.2	619.2	608.5	640.2
	SE	411.8	360.1	316.8	277.2	372.6	276.9	272.2	286.3

Note: Regression equations of comparison: horizontal, $V_g = 1.62 V_e + 1686.30$; $r = 0.86$ and $n = 50$; head-down, $V_g = 1.73 V_e + 1534.48$; $r = 0.91$ and $n = 50$; combined, $V_g = 1.72 V_e + 1468.38$; $r = 0.90$ and $n = 100$.

where T = subject height (meters), and R_0 = whole-body resistance (ohms). Mean values are shown in figure 3. Both the horizontal and head-down subjects exhibited significant decreases in whole-body water during the control period and through day 1 of bed rest, with responses of the two groups being similar. Mean values for the horizontal group started lower and remained lower throughout the period of observation. In the horizontal subjects, whole-body water decreased in a regular manner throughout the bed-rest period and increased slightly during recovery. The head-down group, on the other hand, exhibited a decrease during the first day of bed rest, an increase on day 4, and a decrease thereafter to the end of the bed-rest period. Both groups showed a decrease between tests on the mornings of recovery days 8 and 9 and an increase between the two tests on recovery day 9, with the horizontal subjects exhibiting the greater decrease over that period.

Body composition data for horizontal and head-down subjects are given in tables 24-26. During the control period, U.S. investigators measured the percent body fat of each subject, using the densiometric method described by Keys and Brozek. With this technique, body weight is first measured in air (to within 5 g) and then

with the subject seated on an aluminum weighing seat and suspended in a tank of water (temperature, 36°C). At a signal from the testing personnel, the subject expels all air possible from the lungs, and lowers his head to his legs until his body is in a tucked position and fully immersed. Underwater body weight of each subject was measured repeatedly until the maximal reading was maintained. Residual lung volume was calculated from previously measured vital capacity values, and body density was calculated by the following equation:

$$BD = \frac{W_a}{(W_a - W_w) / D - RV} \quad (11)$$

where

BD body density, g/ml

W_a body weight in air, kg

W_w body weight in water, kg

D density of water, g/ml

RV residual lung volume, liters

Percent body fat was calculated using the following equation:

$$\% \text{ Body fat} = [4.570 / BD - 4.142] \times 100 \quad (12)$$

The weights (kg) of body fat and of lean body mass were calculated from the body weight in air and the percent of body fat. Body density was measured on day 14 of the control period and on days $R + 0$ and $R + 10$ of recovery.

Both groups of subjects had a slight increase (NS) in mean body weight during the 14-day ambulatory control period. Following bed rest, the horizontal subjects exhibited a decrease in mean body weight of 2% ($p < 0.01$) and the head-down group a decrease of 2.9% ($p < 0.01$). Mean body weight of the horizontal subjects remained unchanged on day $R + 10$, but in the head-down group it was 2.2% lower than baseline values ($p < 0.01$).

Percent body fat increased during the ambulatory control period by 2.2% ($p < 0.05$) in the horizontal subjects and by 3.2% ($p < 0.05$) in the head-down subjects. Following bed rest (between days $R + 0$ and $R + 10$), percent body fat decreased in both groups, but the change was not significant.

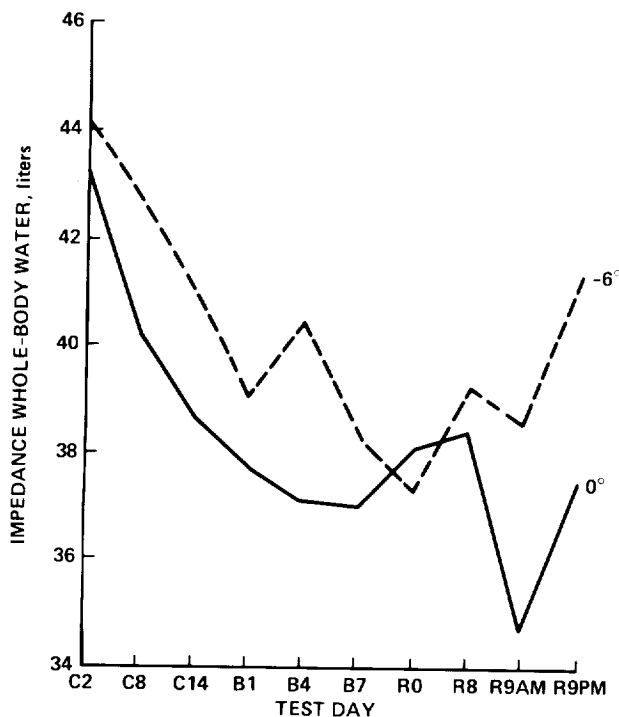


Figure 3.— Whole-body water responses: U.S.

TABLE 24.– MEAN BODY WEIGHT AND FAT

Group	Day			
	Orientation	C-14	R+0	R+10
Mean Body Weight				
Horizontal				
Mean	67 kg	68.3 kg	66.8 kg ^a	68.8 kg ^a
SD	7.3	7.5	7.1	7.1
SE	3.3	3.4	3.2	3.2
-6° tilt				
Mean	69 kg	69.7 kg	67.7 kg ^a	68.2 kg ^a
SD	6.7	6.8	7.1	7.5
SE	3	3	3.2	3.4
Mean Body Fat				
Horizontal				
Mean	15 kg	15.4 kg	15.4 kg	15.3 kg
SD	4.3	4.6	4.5	4.3
SE	1.9	2.1	2	1.9
-6° tilt				
Mean	15.3 kg	15.3 kg	15.4 kg	15.3 kg
SD	4.2	4	4.3	4
SE	1.9	1.8	1.9	1.8

^ap < 0.01 versus control day 14 value.

TABLE 25.– MEAN LEAN BODY WEIGHT AND FAT

Group	Day			
	Orientation	C-14	R+0	R+10
Mean Lean Body Weight				
Horizontal				
Mean	52 kg	52.9 kg	51.4 kg ^a	51.5 kg ^a
SD	6.1	5.6	5.4	5.3
SE	2.7	2.5	2.4	2.4
-6° tilt				
Mean	53.7 kg	54.4 kg	52.3 kg ^a	52.9 kg ^a
SD	6.1	6.5	5.8	6.5
SE	2.7	2.9	2.6	2.9
Mean Body Fat				
Horizontal				
Mean	22.2%	22.4%	22.9%	22.7%
SD	5.5	5.3	5.4	5
SE	2.4	2.4	2.4	2.2
-6° tilt				
Mean	22.1%	21.9%	22.6% ^b	22.4%
SD	5.7	5.4	5.6	5.3
SE	2.6	2.4	2.5	2.4

^ap < 0.01 versus control day 14 value.^bp < 0.05.

TABLE 26.— MEAN BODY WEIGHT: U.S.S.R. SUBJECTS

Group	Day			
	Orientation	C-14	R+0	R+10
Horizontal				
Mean	74.8 kg	70.8 kg	70.2 kg	70.2 kg
SD	6.9	7.2	7.0	7.0
SE	3.4	2.3	2.2	2.2
-6° tilt				
Mean	82.4 kg	75.5 kg	73.9 kg ^a	74.1 kg
SD	6.9	8.4	8.8	8.4
SE	3.4	2.7	2.8	2.7

^ap < 0.01 versus control day 14 value.

Lean body weight increased slightly (NS) in both groups during the control period, but decreased following bed rest by 2.9% ($p < 0.01$) in the horizontal subjects and by 3.9% ($p < 0.01$) in the head-down group. On day R + 10, both groups exhibited a significantly lower ($p < 0.01$) lean body weight, with decreases of 2.6% for the horizontal group and 2.8% for the head-down group.

From the foregoing results, it can be concluded that

1. The observed significant decreases in body weight over the study resulted from a significant decrease in lean body weight, probably because of a loss of body water.

2. The significant increase in percent body fat occurred because absolute body fat (kg) remained constant, whereas total body weight decreased.

3. The larger relative decreases in body weight and lean body weight in the head-down group resulted from the head-down bed-rest position.

U.S.S.R. study—Change in body weight for U.S.S.R. subjects is given in table 26. A significant decrease in body weight occurred for all subjects from the time of orientation until they entered the study. The reasons were not totally clear other than a desire on the part of a number of subjects to engage in more physical activity prior to participating in a study of bed rest effects and its known associated marked hypodynamia. At the end of the pre-bed rest control period there was a significant 4.7-kg difference in body weight between the horizontal and head-down subject groups. This was a much greater response than the 2-kg difference between the same respective groups in the U.S. study. The U.S.S.R. head-down subjects also lost significantly more weight than the horizontal subjects over the course of bed rest and had not regained this weight by the end of the study. This also occurred for U.S. subjects.

Soviet investigators measured volume changes in the arm and leg using occlusion plethysmography (ref. 26).

For the procedures, Whitney strain gauges (mercury in rubber sensors) were applied to the forearm (3 cm below the elbow joint) and to the calf at the largest perimeter. Occlusion was produced by aneroid cuffs capable of increasing pressure to 50 mmHg in 2 to 3 sec; the cuffs were applied to the arm and thigh. Venous occlusion was continued until the resultant curve reached a plateau. Before plethysmography, all subjects were measured for length of the extremities, perimeters of the forearm at spacings of 3 cm, and perimeters of the calf at spacings of 6 cm. Measurement positions were marked with paint so the measurements could be obtained for the same segments in subsequent tests. To further ensure consistency of measurements, they were generally performed by the same investigator (except for forearm measurements on days 5 and 10 of recovery and leg measurements on day 10 of recovery). Plethysmography was performed on day 12 of the control period; on days 2, 4, and 6 of bed rest; and on days 1, 5, and 10 of recovery.

During the procedures, the following data were recorded or measured:

1. Plateau level of the plethysmogram for 2-3-min duration

2. Index of blood flow as determined by the slope of the curve during the first 5 sec (rapid component of volume increase)

3. Blood flow index was expressed in milliliters per minute per 100 ml of tissue

4. Amplitude of the curve from the resting baseline level to the plateau established during occlusion, which was used to determine an index of venous distensibility

5. Rate of volume increase within the first 30 sec of occlusion until the plateau was reached (slow component of volume increase)

6. Extent of volume restoration within 30 sec after the removal of venous occlusion

Plethysmography results are shown in table 27 for both subject groups. Findings during the control period indicated that the horizontal subjects had 157 ml less volume in the forearm and 261 ml less volume in the calf than the head-down subjects. During bed rest, arm volume tended to decrease progressively in both groups and did not vary significantly between them; calf volume on the average decreased by 4.4% in the horizontal subjects and by 6.6% in the head-down group. Both groups showed a significant ($p < 0.05$) decrease in lower leg volume on days 4 and 6 of bed rest and on day 0 of recovery. Although the change was more pronounced in the head-down group, the difference between the two groups was not significant. During the recovery period, leg volumes returned to baseline values in both groups, although arm volumes remained slightly decreased. The decrease in leg volume in both groups by the end of bed rest was similar to changes seen on the fifth day of the Skylab experiment (ref. 2).

Volume rate of blood flow: Baseline values for forearm volume rate of blood flow were somewhat higher for the horizontal subjects than for the head-down subjects, but the difference was not significant (table 28). Flow in the lower legs was essentially the same in both groups. During bed rest, the horizontal subjects exhibited a gradual decrease in forearm and lower-leg rate of blood flow so that by day 6 of bed rest, this variable was substantially lower than baseline values. The head-down subjects also exhibited a decrease, but to a lesser degree, and the change was not significant. This latter group showed a significant decrease in flow to the forearm only on day 0 of recovery, which returned to baseline values by recovery day 10. The findings of decreased peripheral flow in the horizontal subjects correlated with the known decrease in muscular activity during bed rest. By the fifth day of recovery, the head-down subjects exhibited a significantly greater increase in lower leg blood flow than the horizontal group.

Limb volume change with venous occlusion: With venous occlusion during the control period, limb volume increased on the average by 1.7-1.8 ml/100 ml of tissue for the forearm and by 1.9-2.0 ml/100 ml of tissue for the lower leg, with little difference seen between the two groups (table 29). Forearm values for both groups showed little change from baseline levels over the course of bed rest or recovery. The groups showed no significant difference between each other. Lower-leg volume changes, however, were quite different. During bed rest, volume tended to decrease in both groups and was significantly lower ($p < 0.05$) in the horizontal subjects beginning on the second day of bed rest. By the first day of recovery,

the decrease in lower-leg volume became significant in both groups. These changes with venous occlusion were thought to reflect reduced venous tone (capacity) associated with restricted mobility. In addition, it was felt that the observed findings might be indirectly related to extravascular fluid reabsorption in leg tissues. By the second day of bed rest, lower-leg findings in the horizontal subjects significantly decreased toward normal and tended to decrease in the head-down group. This apparent reduction in filtration processes (loss of extracellular fluid reabsorption) agrees with previous findings for humans and animals that the number of perfused capillaries is reduced during restricted muscular activity.

On termination of venous occlusion, volume was restored to baseline levels in both groups within 30 sec or less, both during and after bed rest.

A number of investigators have demonstrated that the regulation of vascular tone is clearly associated with the level and magnitude of intravascular pressure and the magnitude of transmural pressure (refs. 2 and 27). These findings would suggest that vascular tone should be decreased in head-down subjects since hydrostatic (hence transmural) pressure for the lower extremities is reduced in this body position. It is hypothesized that basal arterial tone is reduced to facilitate lower extremity blood flow. As a result of the body's adaptation to reduced muscular activity, the volume rate of blood flow to the lower extremities is also reduced. The interaction of these two processes could explain the less pronounced lowering of the volume rate of blood flow to the lower legs in the head-down subjects than was seen in the horizontal group.

Finally, recumbency in the head-down position should create the following physiologic responses: (1) reduced venous pressure in the veins of the lower limbs, (2) increased drainage of blood from the limbs, and (3) reduced pressure between the tissues. As a result of these changes, large-vessel tone should be reduced. However, restricted muscular activity is usually accompanied by an increase in large-vessel tone of the lower leg. In the present study, the interaction of these various effects resulted in a less pronounced lowering of vessel tone in the head-down subjects than in the horizontal group.

Comparison of U.S. and U.S.S.R. Findings

Electrophysiology at rest- The electrocardiographic findings of the two teams of investigators were in complete agreement. Neither team observed any significant changes in either the horizontal or head-down subjects.

TABLE 27.— VOLUME CHANGES IN THE FOREARM AND LOWER LEG (ml) DURING PLETHYSMOGRAPHY AT REST: U.S.S.R. STUDY

		Control- period mean	Bed-rest day			Recovery day		
			2	4	6	R + 0	R + 5	R + 10
Forearm								
Horizontal	Mean	1025.8	1015.3	1010.4	1019.5	1008.1	987.8	1013.9
	SD	109.2	106.9	88.5	91.1	87.6	84.3	83.3
	SE	48.8	47.8	39.6	40.8	39.2	37.7	37.3
Head-down	Mean	1183.0	1203.3	1185.7	1162.6	1168.9	1163.5	1150.8
	SD	92.4	103.5	118.8	110.2	114.8	108.5	101.4
	SE	41.3	46.3	53.1	49.3	51.3	48.5	45.4
Lower leg								
Horizontal	Mean	2415.9	2343.8	2382.2	2309.4	2300.1	2398.0	2412.2
	SD	236.3	265.3	253.2	231.8	224.4	217.2	269.0
	SE	105.7	118.6	113.2	103.6	100.4	97.1	120.3
Head-down	Mean	2677.4	2578.2	2588.5	2508.3	2534.6	2602.8	2609.6
	SD	268.5	245.8	263.4	226.9	265.4	241.6	306.4
	SE	120.1	109.9	117.8	101.5	118.7	108.0	137.0

TABLE 28.— CHANGES IN VOLUME RATE OF BLOOD FLOW (ml/100 ml tissue) IN THE FOREARM AND LOWER LEG DURING PLETHYSMOGRAPHY AT REST: U.S.S.R. STUDY

		Control- period mean	Bed-rest day			Recovery day		
			2	4	6	R + 0	R + 5	R + 10
Forearm								
Horizontal	Mean	6.99	5.40	3.79 ^a	3.36 ^a	4.08	3.96	7.32
	SD	3.63	4.14	2.90	1.57	3.16	1.97	2.56
	SE	1.63	1.85	1.30	0.70	1.41	0.88	1.15
Head-down	Mean	6.3	6.00	5.64	4.23	2.16 ^a	5.52	7.50
	SD	3.44	1.64	2.19	0.95	0.91	5.27	5.21
	SE	1.54	0.74	0.98	0.43	0.41	2.36	2.33
Lower leg								
Horizontal	Mean	2.43	2.21	0.66 ^a	1.41 ^a	1.54 ^a	2.26	2.35
	SD	0.57	0.43	0.26	0.91	0.53	0.32	0.60
	SE	0.25	0.19	0.12	0.41	0.24	0.14	0.27
Head-down	Mean	2.48	2.40	1.77	2.08	2.04	3.73	3.95
	SD	1.07	0.85	0.57	0.46	0.68	1.18	1.64
	SE	0.48	0.38	0.25	0.21	0.31	0.53	0.73

^aSignificant difference.

TABLE 29.- VOLUME INCREASE IN THE FOREARM AND LOWER LEG (ml/100 ml tissue) WITH OCCLUSION (50 mmHg) OF THE VEINS: U.S.S.R. STUDY

		Control-period mean	Bed-rest day			Recovery day		
			2	4	6	R + 0	R + 5	R + 10
Forearm								
Horizontal	Mean	1.70	1.49	1.42	1.77	1.50	1.50	1.66
	SD	0.53	0.33	0.50	0.32	0.52	0.61	0.52
	SE	0.24	0.15	0.23	0.14	0.24	0.27	0.23
Head-down	Mean	1.79	1.87	1.82	1.52	1.54	1.18	1.61
	SD	0.23	0.36	0.35	0.63	0.42	0.36	0.63
	SE	0.10	0.16	0.16	0.28	0.17	0.16	0.28
Lower leg								
Horizontal	Mean	2.08	1.22 ^a	1.15 ^a	1.38 ^a	1.22 ^a	1.26 ^a	1.66
	SD	0.64	0.33	0.33	0.26	0.37	0.50	0.53
	SE	0.29	0.15	0.15	0.12	0.17	0.23	0.24
Head-down	Mean	1.87	1.60	1.56	1.51	1.23	1.94	1.92
	SD	0.78	0.84	0.74	0.48	0.65	0.54	0.71
	SE	0.35	0.37	0.33	0.22	0.28	0.24	0.32

^aSignificant difference.

Echocardiography at rest— Echocardiographic procedures of the U.S. and U.S.S.R. investigators did not differ significantly. Variations consisted of

1. U.S. investigators performed baseline echocardiographic measurements on days 2 and 13 of the control period, whereas U.S.S.R. investigators performed them on control days 13 and 14.

2. U.S. investigators recorded resting echos four times on the first day of bed rest, whereas U.S.S.R. investigators recorded them three times on that day.

3. The U.S. study included VCF recordings; the U.S.S.R. study did not. The U.S. control data obtained after 11 days of subject confinement showed consistent decreases in all subjects by the second measurement and suggested that some degree of deconditioning occurred during the 14-day ambulatory control period.

U.S. and U.S.S.R. data at rest are compared for the horizontal subjects in figures 4(a)-4(g) and for the head-down subjects in figures 5(a)-5(g). U.S. and U.S.S.R. resting echocardiographic values differed in several areas. U.S.S.R. calculated values for EDV, ESV, SV, and CO

exceeded U.S. values in all cases and significant differences were noted as follows:

1. End diastolic volume for the first, second ($p < 0.05$), and third readings on day 1 of bed rest and day 2 of bed rest ($p < 0.01$) (see figs. 4(c) and 5(c))

2. End systolic volume for day 1 of control ($p < 0.05$), the second ($p < 0.05$), and third ($p < 0.01$) readings on day 1 of bed rest, and day 2 of bed rest ($p < 0.01$) (see figs. 4(d) and 5(d))

3. Stroke volume for the first ($p < 0.05$) and third ($p < 0.01$) readings on day 1 of bed rest (see fig. 5(e))

4. Cardiac output for the third reading on days 1 and 2 of bed rest and on day 5 of recovery ($p < 0.05$) (see fig. 5(f))

5. Ejection fraction during the second reading ($p < 0.05$) on day 1 of bed rest (see fig. 5(g))

Because of the differences between the two sets of results, it was felt inadvisable to pool data from the two investigations to obtain mixed (U.S./U.S.S.R.) data for comparing the two sets of horizontal and head-down subjects.

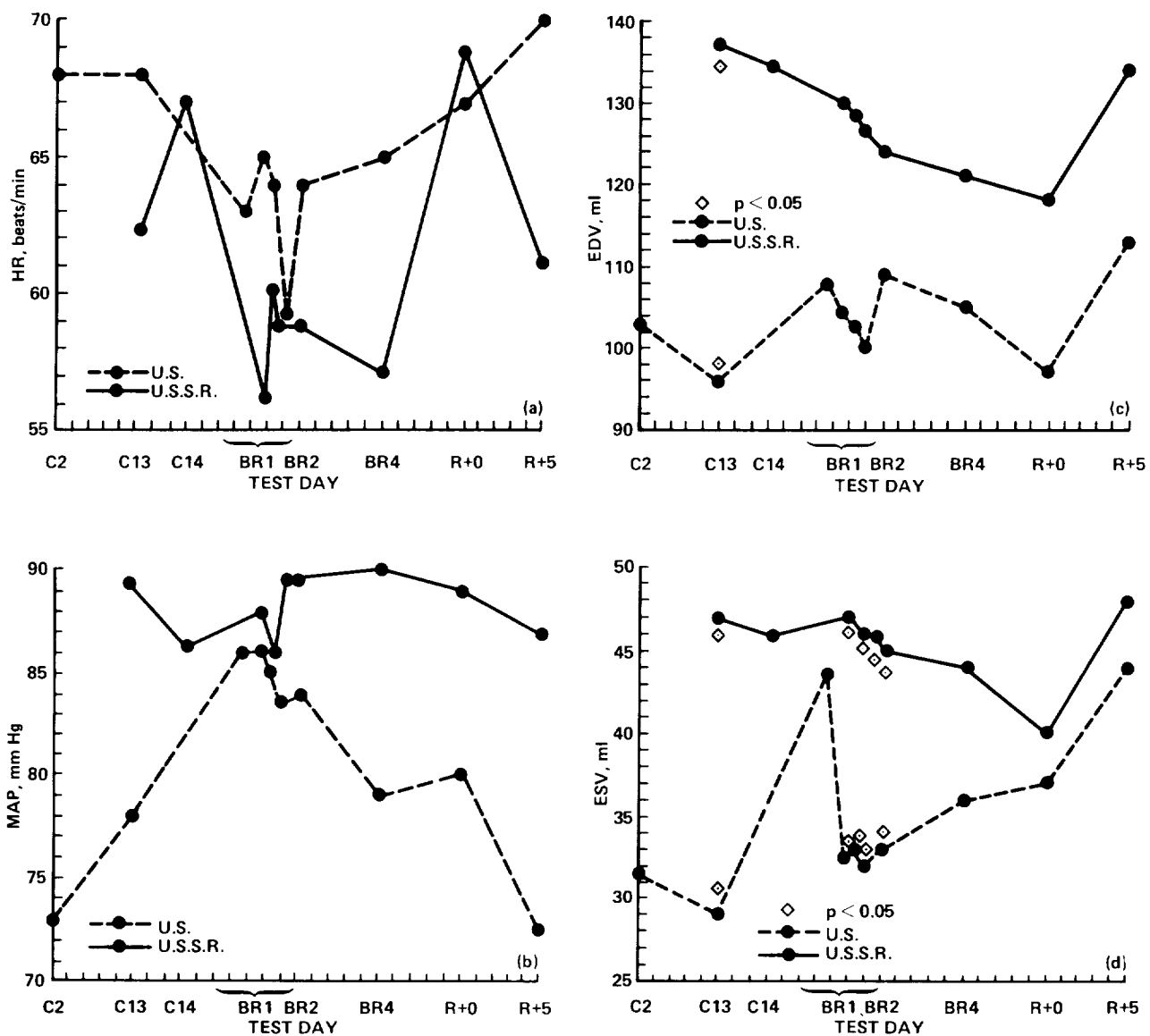


Figure 4.— Dynamics of echocardiography in horizontal subjects at rest: comparison of U.S. and U.S.S.R. findings.
 (a) Heart rate. (b) Mean arterial pressure. (c) End diastolic volume. (d) End systolic volume.

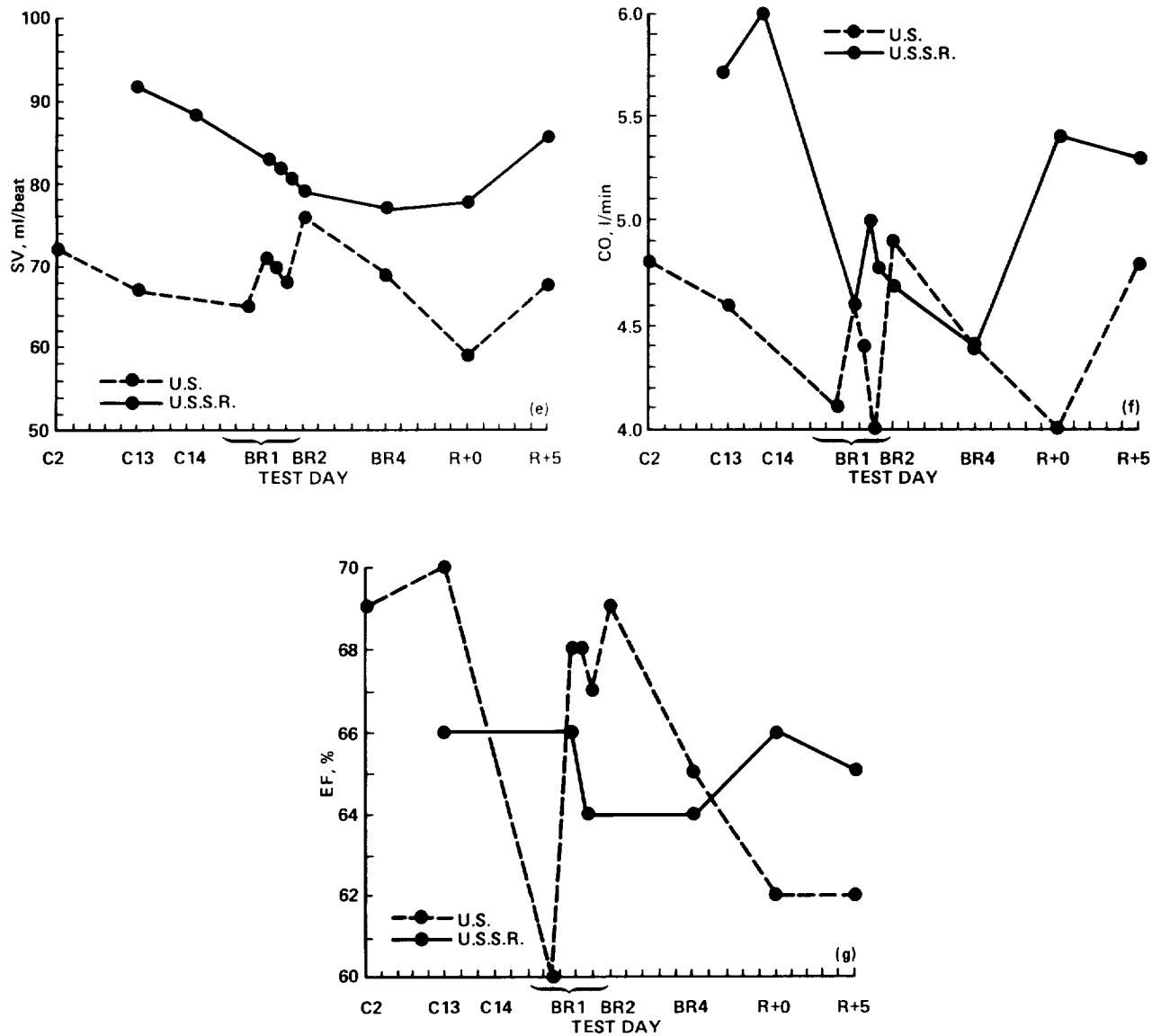


Figure 4.- Concluded. (e) Stroke volume. (f) Cardiac output. (g) Ejection fraction.

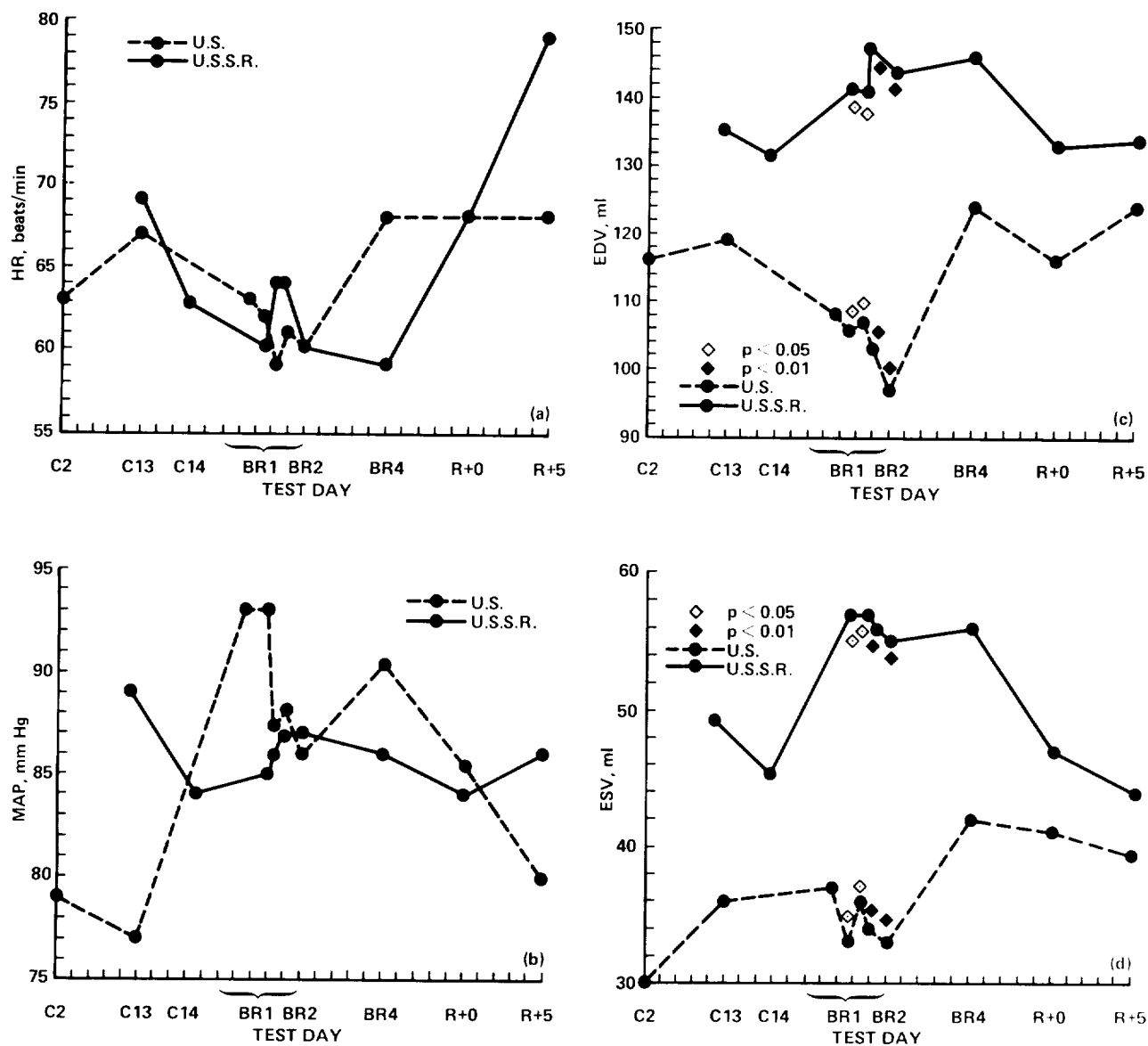


Figure 5.— Dynamics of echocardiography in antiorthostatic (-6° head-down) subjects at rest: comparison of U.S. and U.S.S.R. findings. (a) Heart rate. (b) Mean arterial pressure. (c) End diastolic volume. (d) End systolic volume.

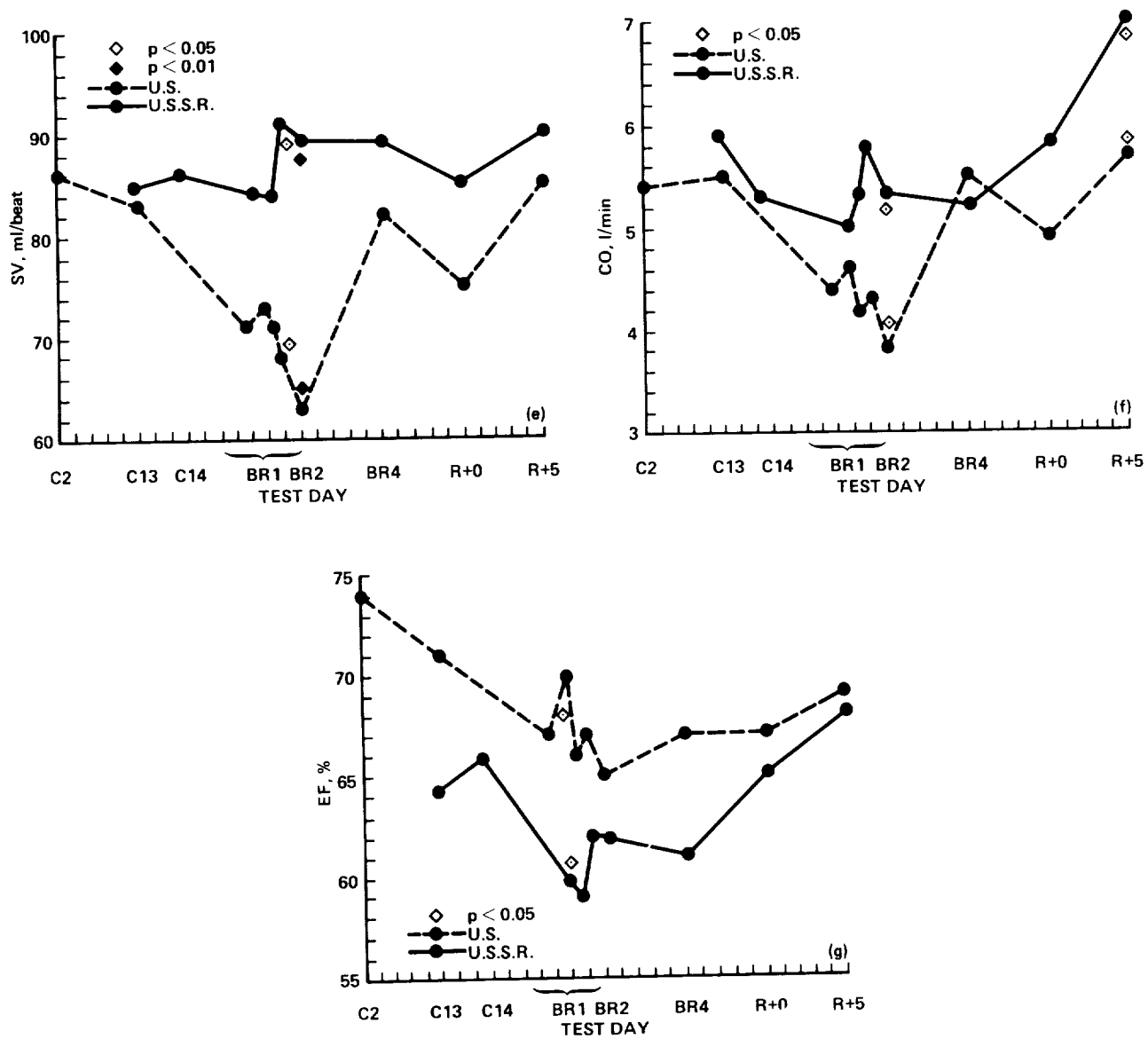


Figure 5.— Concluded. (e) Stroke volume. (f) Cardiac output. (g) Ejection fraction.

Lower-body negative pressure—Mean values for all parameters at rest, peak LBNP, and the differences induced by 50-mmHg negative pressure are given in table 30. Comparisons of LBNP findings for systolic and diastolic blood pressure for respective horizontal and head-down subjects are also given in figures 6(a) and 6(b) and 7(a) and 7(b). These overall findings, as indicated earlier, were obtained on the U.S. side by using a lower body decompression chamber and by wearing a CHIBIS suit by U.S.S.R. investigators. Heart rate for horizontal subjects showed little difference between the teams before and during LBNP stress except for day 5 of recovery when U.S. values were lower. U.S. values tended to be lower for all other parameters—SBP, PP, EDV, ESV, SV, and CO, including DBP, which was significantly lower ($p < 0.05$, fig. 6(b)). EF proved to be variable. Head-down subjects showed no differences for HR or SBP (figs. 7(a)), but all other parameters again tended to be lower for U.S. subjects. As was the case for horizontal subjects, DBP was significantly lower in U.S. subjects (fig. 7(b)).

The reason for the significant differences for PP between the U.S. and U.S.S.R. subjects related to the consistently lower recorded diastolic blood pressures in the U.S. study. PP for U.S.S.R. subjects, which tended to approximate pre-LBNP U.S. values (see table 30), decreased to approximately 40-50% of resting levels with peak LBNP. This did not occur for the U.S. study. Thus, resulting LBNP-induced PP change for U.S.S.R. subjects was 19-62% greater. Despite the above-noted differences in diastolic pressure, these values regularly increased with application of LBNP following bed rest, suggesting that an elevated peripheral vascular resistance is associated with the deconditioning process.

Several factors may have contributed to the observed differences in U.S. and U.S.S.R. blood pressure findings. First, the two teams used different equipment and techniques for measuring blood pressure. Second, U.S.S.R. investigators used the single lowest PP obtained during LBNP in their calculations, whereas U.S. investigators averaged the data for the final 5-min period of peak LBNP stress. Finally, the U.S. subjects showed a distinct tendency for lowering of DBP over the pre-bed rest ambulatory control period, indicating some degree of change in physiologic state for this group during this period.

End-diastolic volumes, SV and CO tended to be higher for U.S.S.R. subjects (see table 30). Still, observed

comparative LBNP-induced differences were not of note except for the greater fall in EDV for U.S.S.R. horizontal subjects during control (52 vs 34 ml) and a smaller decrease for U.S.S.R. head-down subjects immediately after bed rest (43 vs 63 ml). Similar differences in EDV were reflected in much greater post-bed rest decreases in SV (53 vs 38 ml/beat) and CO (1.9 vs 0.4 L/min) for U.S. head-down subjects. In addition, LBNP induced 1.8 L/min and 2.1 L/min decreases in CO for respective U.S. horizontal and head-down subjects on day 5 of recovery, while comparable changes for U.S.S.R. subjects were 20% of these values. In the U.S. study, head-down subjects experienced a significantly greater decrease in EDV following bed rest than did the horizontal subjects (64 ml vs 38 ml, see table 30). Since bed-rest-induced intravascular volume losses were similar in the two groups, changes suggest that the peripheral vascular mechanisms affecting venous return may have been altered because of the head-down bed-rest position. Such changes did not occur for the U.S.S.R. study.

In the U.S. study the observed immediate post-bed rest decrease in cardiac output with peak LBNP (-2 L/min) in the head-down subjects was significantly larger than that seen in the horizontal subjects. This decrease, which was more than twice that seen before bed rest, persisted throughout the recovery period. Horizontal subjects showed a similar decrease on recovery day 5. Such changes were of a smaller magnitude (half or less) in the U.S.S.R. study (see table 30). As would be expected, with LBNP stress, both sets of investigators found that EDV and SV decreased with increased HR. Both groups noted significantly increased heart rates during LBNP testing which was exaggerated immediately following bed rest. The large decrements in EDV, ESV, and SV observed in U.S. subjects between average control-period values and values measured on day 5 of recovery suggest that both subject groups may have experienced continued deconditioning.

The difference in response of EF and VCF for the two U.S. groups and EF for the U.S.S.R. groups (table 30) suggests that the head-down group experienced a greater degree of myocardial deconditioning.

Finally, a change in MAP does not appear to offer a sufficient explanation for observed changes in EDV, SV, and CO, since there was hardly any change for U.S. subjects and the value rose only 3 to 4 mmHg for U.S.S.R. subjects.

TABLE 30.- HEMODYNAMIC CHANGES WITH -50 mmHg LBNP

	U.S. data								U.S.S.R. data					
	Pre-bed rest		Post-bed rest						Pre-bed rest		Post-bed rest			
	Day 0		Day 5		Day 10		Day 0		Day 5					
	0°	-6°	0°	-6°	0°	-6°	0°	-6°	0°	-6°	0°	-6°	0°	-6°
Control														
HR	68	64	68	58	71	68	72	68	67	66	67	66	79	65
EDV	100	117	97	116	113	124	106	123	138	132	122	127	128	133
ESV	31	33	37	41	44	39	39	40	46	47	45	40	44	43
SV	70	85	59	85	68	85	67	84	92	85	77	87	84	90
CO	4.7	5.5	4.0	4.9	4.8	5.7	4.8	5.6	6.2	5.6	5.2	5.7	6.6	5.9
EF	0.69	0.73	0.62	0.67	0.62	0.69	0.63	0.68	0.67	0.64	0.63	0.69	0.66	0.68
VCF	1.76	1.79	1.51	1.73	1.48	1.73	1.53	1.70	-	-	-	-	-	-
PP	55	60	51	61	51	58	48	57	41	37	44	46	38	45
MAP	74	81	78	83	73	80	77	79	91	94	93	91	87	87
-50 mmHg LBNP														
HR	86	83	102	92	89	83	101	85	91	94	102	112	104	92
EDV	66	77	59	52	57	68	63	75	86	95	71	84	84	83
ESV	21	20	23	19	23	25	20	28	32	38	33	39	28	31
SV	45	57	37	32	34	43	43	47	54	57	38	45	56	52
CO	3.9	4.8	3.8	3.0	3.0	3.6	4.3	4.0	4.9	5.4	3.9	5.2	5.8	4.8
EF	0.69	0.74	0.62	0.63	0.60	0.65	0.69	0.65	0.64	0.60	0.54	0.54	0.67	0.63
VCF	1.99	2.26	1.73	1.82	1.68	1.79	2.08	1.82	-	-	-	-	-	-
PP	42	48	39	46	38	50	34	44	22	19	14	26	22	24
MAP	74	81	79	86	73	83	74	80	95	93	95	94	83	89
Δ due to -50 mmHg LBNP														
HR	18	19	34	34	18	15	29	17	24	28	35	46	25	27
EDV	34	40	38	64	56	56	43	48	52	37	51	43	44	50
ESV	10	13	14	9	21	14	18	12	14	9	12	1	16	12
SV	25	28	22	53	34	42	24	37	38	28	39	42	28	38
CO	0.8	0.7	0.2	1.9	1.8	2.1	0.5	1.6	1.3	0.2	1.3	0.5	0.8	1.1
EF	0	0.01	0	0.04	0.02	0.04	0.06	0.03	0.02	0.08	0.09	0.15	0.01	0.05
VCF	0.23	0.47	0.22	0.09	0.20	0.06	0.55	0.12	-	-	-	-	-	-
PP	13	12	12	15	13	8	14	13	19	18	30	20	16	21
MAP	0	0	1	3	0	3	3	1	4	1	2	3	4	2

Note: HR - bpm; EDV, ESV, SV - ml; CO - L/min; EF - %; VCF - cm/sec; PP, MAP - mmHg.

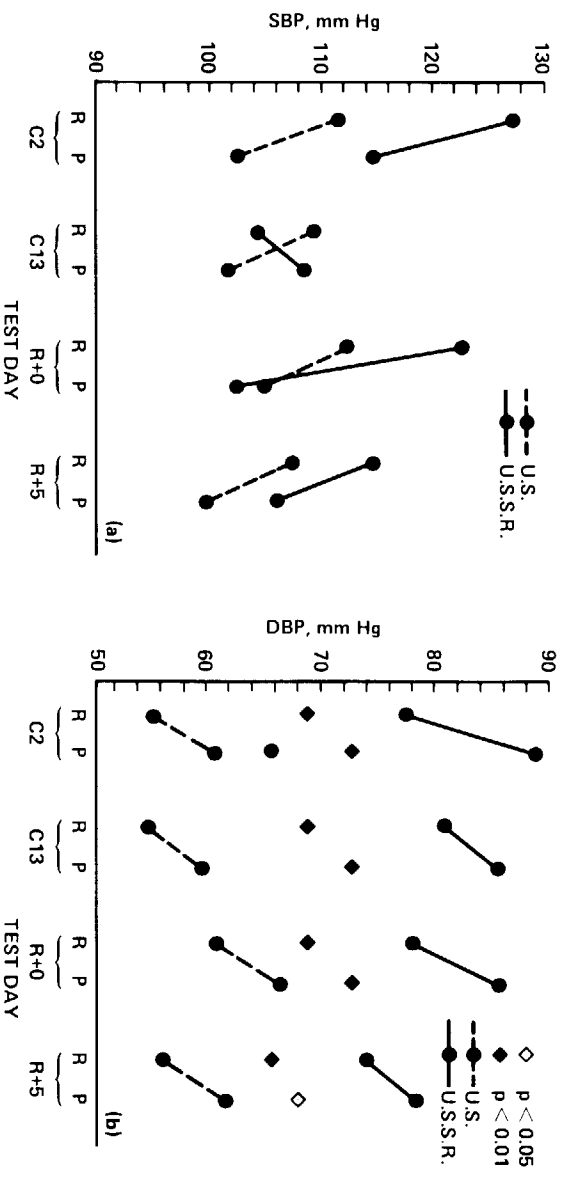


Figure 6.— Comparison of hemodynamics at rest (R) and peak (P) LBNP in U.S. and U.S.S.R. horizontal bed-rest subjects. (a) Systolic blood pressure. (b) Diastolic blood pressure.

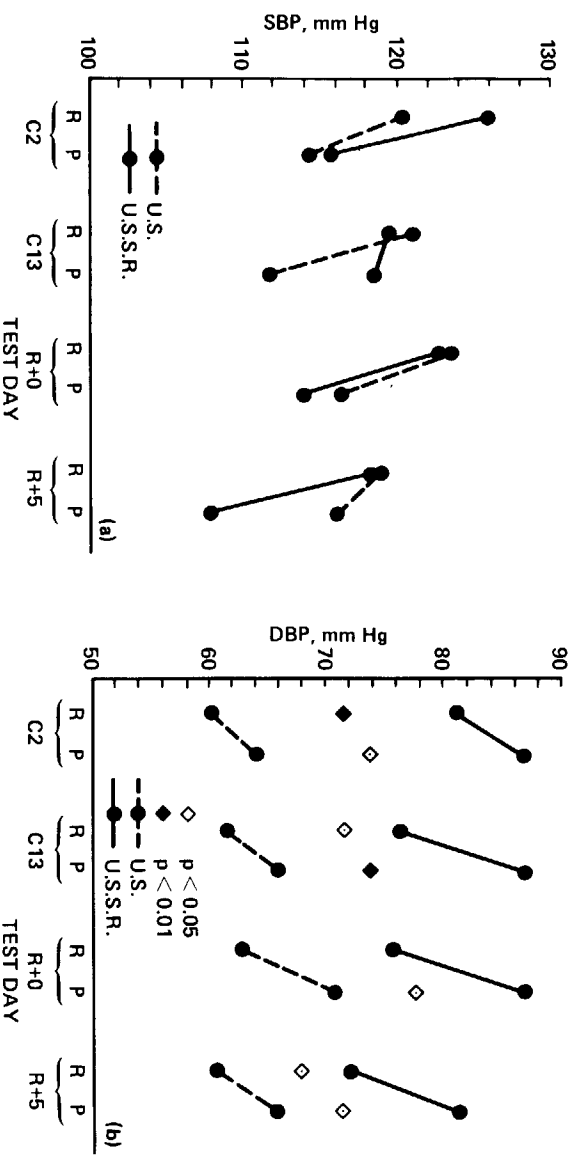


Figure 7.— Comparison of hemodynamics at rest (R) and peak (P) LBNP in U.S. and U.S.S.R. head-down subjects. (a) Systolic blood pressure. (b) Diastolic blood pressure.

The data in table 30 generally support the conclusion that head-down subjects showed greater degradations in response to LBNP than did horizontal subjects, with U.S. subjects doing so to a greater extent than U.S.S.R. subjects. However, test results were not closely comparable between the two groups. It appeared that -50 mmHg LBNP experienced in a CHIBIS suit produced greater increases in HR and decreases in EDV, yet calculated SVs were similar to U.S. values. These latter differences may have been due to difficulties in obtaining good-quality echocardiographic images and in the ease of making required measurements. The small number of subjects, particularly for the U.S.S.R. group, undoubtedly also contributed. As already mentioned, some mild degree of deconditioning from pre-bed rest confinement may also have been present for U.S. subjects.

U.S. findings related to resting heart volume data over the course of bed rest showed that all subjects tended to exhibit a decrease in EDV and ESV through day 2 of bed rest, findings consistent with a decrease in plasma volume. This was followed by an increase in these variables from day 2 through day 4 of bed rest in head-down U.S. subjects, whereas the U.S.S.R. head-down subjects showed a continued increase from day 1 through day 4 of bed rest. Thereafter, the head-down subjects in both studies exhibited decreases in EDV through the end of bed rest.

The findings in the present study did not support results from previous research related to STIs because bed rest did not induce significant changes (ref. 2). The present findings, however, are consistent with echocardiographic results obtained during this study, which demonstrated that no significant changes occurred in SV at rest for either of the subject groups—a change which had been usually observed in previous studies. Similarly, results of the present study during LBNP did not agree with previous findings of significant changes in STI following bed rest, although again they were consistent with echocardiographic findings of the present study. To date, the reasons for the differences are unclear.

Plethysmography—Although the U.S. team used impedance plethysmography and the U.S.S.R. team used occlusion plethysmography, and although the types of measurements differed between the two, the findings correlated fairly well ($r = 0.90$ to 0.99 ; $p < 0.05$) for the individual subjects, for each group, and for all combined. Comparison of findings for horizontal subjects is given in table 31 and for the head-down subjects in table 32. In general, volume increases and blood pooling values were smaller in the U.S. subjects than in the U.S.S.R. subjects. Both teams of investigators found that the observed

changes occurred very gradually in all subjects. They also concluded the following:

1. LBNP increased lower-body volume to similar degrees.
2. There were generally no consistent differences in plethysmographic responses during LBNP in the horizontal and head-down subjects, either before or immediately after bed rest.
3. There were no changes in vascular compliance as a result of 7 days of bed rest.
4. Leg-volume enlargement persisting for as long as 5 min after release of suction suggested that extravascular fluid accumulation was a feature of the physiologic response.

In the U.S. horizontal subjects, there was a tendency during the second of the control-period measurements for volume decreases in the upper and lower extremities, which continued, but at a slower rate, during bed rest. Evidence of such changes in the ambulatory control period suggests that confinement itself may play a role in deconditioning. In this group, on the other hand, pelvic and torso volumes increased during control and persisted during bed rest. Although the increase in pelvic volume in this group persisted throughout bed rest, torso volume decreased during the last 4 days of bed rest. The latter data were consistent with echocardiographic findings of EDV changes in these subjects. The general trend of plethysmographic changes during bed rest for U.S. head-down subjects was consistent with echocardiographic findings, which initially demonstrated a decrease, then an increase in EDV in this group. In fact, the differences in torso volume changes between the horizontal and head-down groups, as measured by plethysmography, were generally reinforced by the echocardiographic results.

V. CLINICAL LABORATORY STUDIES

Both U.S. and U.S.S.R. space crews have exhibited specific metabolic and hormonal changes following exposure to weightlessness. Investigators from the two nations have conducted numerous ground-based studies using various simulation techniques in an attempt to identify the mechanisms underlying these changes. Horizontal bed rest has been the primary method used to study the causes of endocrine and hormonal changes occurring during spaceflight. Although ground-based studies have shown that hormones play an important part in physiological changes during bed rest, these studies as yet have not identified the mechanisms responsible (ref. 29).

TABLE 31.— COMPARISON OF LEG VOLUME FINDINGS IN HORIZONTAL SUBJECTS (0°):
U.S. AND U.S.S.R. STUDIES^a

Time, min	Last minute				30 sec	1 min	5 min	Regression equations
LBNP, mmHg	-25	-35	-40	-50	Release			U.S. vs U.S.S.R. data
Control period								U.S. = 0.42R - 0.03 r = 0.97
Control average: day 2 and day 13								
U.S.S.R.	1.960	2.720	3.320	3.840	1.480	1.140	0.940	
	0.780	0.887	0.487	0.627	0.363	0.313	0.397	
U.S.	0.74	1.00	1.36	1.74	0.53		0.53	
	0.21	0.30	0.40	0.50	0.26		0.17	
t-test value	3.02 ^b	3.67 ^b	6.22 ^b	5.24 ^b	4.26 ^b		1.90	
Recovery day 0								
U.S.S.R.	1.660	2.420	3.220	4.440	1.960	1.000	0.640	
	0.196	0.217	0.427	0.635	0.695	0.436	0.351	
U.S.	0.79	1.11	1.49	1.95	0.76		0.54	
	0.21	0.27	0.36	0.40	0.49		0.16	
t-test value	6.07 ^b	7.56 ^b	6.20 ^b	6.64 ^b	2.82 ^b		0.52	U.S. = 0.39R + 0.16 r = 0.98
Recovery day 5								U.S. = 0.41R - 0.07 r = 0.97
U.S.S.R.	2.040	2.800	3.460	4.140	1.760	1.040	0.860	
	0.921	0.970	1.220	1.113	0.623	0.669	0.319	
U.S.	0.73	0.93	1.33	1.79	0.60		0.42	
	0.20	0.27	0.21	0.27	0.36		0.29	
t-test value	2.78 ^b	3.71 ^b	3.44 ^b	4.10 ^b	3.22 ^b		2.04	
Recovery day 10								
U.S.S.R.	2.240	3.160	3.780	4.600	1.640	1.160	0.820	
	0.518	0.856	0.820	0.731	0.456	0.860	0.867	
U.S.	0.88	1.14	1.48	1.81	0.58		0.41	
	0.18	0.24	0.22	0.17	0.30		0.27	
t-test value	4.96 ^b	4.54 ^b	5.42 ^b	7.43 ^b	3.88 ^b		0.90	U.S. = 0.38R + 0.03 r = 0.99

Note: Total for all values in this table: U.S. = 0.39R + 0.04, r = 0.97.

^aValues shown are milliliters per 100 ml; $\bar{x} \pm \text{SD}$.

^bp < 0.05 U.S.S.R. values versus U.S. values.

TABLE 32.— COMPARISON OF LEG VOLUME FINDINGS IN HEAD-DOWN (–6°) SUBJECTS:
U.S. AND U.S.S.R. STUDIES^a

Time, min	Last minute				30 sec	1 min	5 min	Regression equations	
LBNP, mmHg	-25	-30	-40	-50	Release			U.S. vs U.S.S.R. data	
Control period	Control average: day 2 and day 13							U.S. = 0.32R + 0.41 r = 0.92	
U.S.S.R.	1.620 0.482	2.680 0.936	3.220 1.192	4.120 1.472	1.520 1.099	0.900 0.863	0.720 0.801		
U.S.	0.81 0.35	0.99 0.48	1.51 0.48	1.90 0.53	0.96 0.24		0.81 0.24		
t-test value	2.72 ^b	3.21 ^b	2.66 ^b	2.84 ^b	1.00 ^b	-0.22			
Recovery day 0									U.S. = 0.34R + 0.55 r = 0.94
U.S.S.R.	2.020 1.158	2.740 1.014	3.720 0.795	4.760 0.945	1.760 0.415	0.900 0.224	0.720 0.421		
U.S.	0.99 0.55	1.39 0.60	1.81 0.62	2.28 0.68	1.09 0.29		1.04 0.24		
t-test value	1.61	2.29	3.79 ^b	4.26 ^b	2.65 ^b		-1.32		
Recovery day 5									
U.S.S.R.	2.080 0.642	2.860 0.888	3.520 0.944	4.360 1.004	1.400 0.600	0.860 0.537	0.620 0.492		
U.S.	0.83 0.40	0.95 0.60	1.46 0.72	1.95 0.83	0.79 0.44		0.76 0.44		
t-test value	3.31 ^b	3.56 ^b	3.47 ^b	3.55 ^b	1.64		-0.42		
Recovery day 10								U.S. = 0.42R + 0.30 r = 0.91	
U.S.S.R.	2.500 0.503	3.150 0.854	3.700 0.931	4.400 1.143	1.525 1.135	1.150 1.320	1.000 1.275		
U.S.	0.98 0.45	1.40 0.62	1.86 0.76	2.44 0.83	1.05 0.35		0.92 0.41		
t-test value	4.50 ^b	3.32 ^b	3.06 ^b	2.78 ^b	0.80 ^b		0.13		

Note: Total for all values in this table: U.S. = 0.35R + 0.39, r = 0.89.

^aValues shown are milliliters per 100 ml; $\bar{x} \pm \text{SD}$.

^bp < 0.05 U.S.S.R. values versus U.S. values.

The adrenal-pituitary system contributes significantly to maintaining homeostasis during stressful or unusual situations. Responses of this system to bed rest generally have been studied by measuring urinary excretion of 17-hydroxycorticosteroid (17-OHCS) and 17-ketosteroid concentrations. But changes in these variables have been inconsistent from study to study. Some investigators have found no change in 17-ketosteroids, but a significant increase in 17-OHCS; others have found the reverse. However, studies of urinary cortisol excretion have consistently shown an increase during bed rest and an even greater increase during ambulatory recovery. Investigators using serum levels of adrenocorticotrophic hormone (ACTH) and cortisol found that ACTH increased gradually from the beginning of bed rest, rose sharply after 30 days, and gradually returned to control levels after bed rest. Conversely, blood cortisol levels were decreased throughout bed rest (ref. 1).

With spaceflight and bed rest, there is a redistribution of extravascular fluid to vascular space and a redistribution of blood volume, accompanied by a compensatory loss of water, potassium, and sodium as the hormonal and renal mechanisms are activated to prevent vascular volume from increasing beyond limits established by the receptors. Blood-volume shifts are accompanied by changes in aldosterone and antidiuretic hormone (ADH) and plasma renin activity. Aldosterone, the salt-retaining hormone of the adrenal cortex, has been observed to decrease during bed rest, often almost immediately after bed rest is begun. This change has been interpreted to be the initial response to redistribution of blood volume. But findings on aldosterone change have varied, with some investigators observing increases, slight decreases, or no change with bed rest (refs. 1, 29, and 30). Plasma renin activity increases constitute an early indication of altered neural and circulatory conditions. Such changes are interpreted as the body's attempt to maintain adequate renal blood flow. But findings on this variable have differed, with some investigators finding little change and others an increase. On the other hand, serum measurements have consistently shown that ADH decreases during bed rest, and urinary measurements have shown that it varies. Limited postflight measurements have shown increases in ADH in both serum and urine.

An early diuresis accompanied by a loss of electrolytes has been observed consistently with bed rest and immersion. This change occurs as the body attempts to maintain vascular-extravascular equilibrium. It would seem that when equilibrium is achieved as bed rest continues, fluid shifts and loss of vascular fluid volume would no longer occur. However, investigators have demonstrated consistently that the loss of vascular fluid continues (ref. 2). The underlying mechanisms are not completely understood, but it is hypothesized that any of

three conditions could occur: (1) vascular fluid is excreted, (2) fluid is transferred from vascular to extravascular space, or (3) fluid transfers through extravascular space to intracellular space. To evaluate these hypotheses, investigators have studied changes in plasma volume, extracellular water, and total body water.

It has long been known that prolonged bed rest is accompanied by a decrease in circulating plasma volume (ref. 2). The decrease can range from 5% to 20%, depending on the length of bed rest and on the study design. Plasma volume in the normal male is about 40 ml/kg of body weight; for a male weighing 80 kg, for example, the loss in plasma volume during prolonged bed rest would amount to 160-640 ml. Loss of plasma volume begins during the first 24 hr of bed rest, reaches a mean loss of 10% by 48 hr, and then continues more slowly, reaching a loss of about 20% after 30 days. During this period of change, there usually is no change in electrolyte and protein concentrations. Similarly, blood pressure is maintained despite a reduction in circulating blood volume, suggesting that vascular volume decreases proportionally to blood volume decrease, which in turn results from a decrease in plasma volume.

The decrease in circulating blood volume usually stimulates the vascular tree to release catecholamines. Therefore, it would be expected that catecholamines would increase during bed rest. But findings to date have not demonstrated that catecholamine activity does increase, although the accelerated HR seen with bed rest may be an indirect indicator of such occurrence.

Extracellular fluid consists of circulating plasma and interstitial fluid, with plasma volume amounting to one half of interstitial fluid. Plasma volume decreases during bed rest; therefore, extracellular fluid also should decrease unless the plasma volume decrease represents only a transfer of water, protein, and electrolytes into the interstitial space. But the diuresis associated with the decrease in plasma volume argues against such a shift. Extracellular fluid volume has been measured in only a few bed-rest studies (ref. 2). Findings have been variable, with some investigators finding no decrease in extracellular fluid volumes despite a decrease in plasma volume, others observing a decrease greater than the plasma volume decrease, others finding equal decreases in both, and still others finding that extracellular fluid volume actually increased. With regard to the last finding, a decrease in plasma volume accompanied by an increase in extracellular fluid volume would indicate that body water was shifted from the intravascular compartment to the extracellular compartment. In most bed-rest studies, a greater percentage decrease in plasma volume has been observed than would be expected from increases seen in peripheral hematocrit, thus indicating a change in the ratio of total body hematocrit to peripheral hematocrit (ref. 31).

Whether interstitial fluid changes during bed rest is not well studied. Findings from spaceflight (refs. 32 and 33) have indicated that fluid losses during short-term flights have resulted in a loss of extracellular fluid; in longer flights, losses in extracellular fluid probably are gradually restored, but there is still an overall loss because of muscular atrophy.

Total body water also changes during spaceflight and bed rest. This element consists of extracellular and intracellular water and is proportional to lean body mass. Changes in lean body mass and in total body water are interrelated because adipose tissues contain no water unless they replace lean tissue. Thus, if lean body mass decreases, total body water can be expected to decrease. At present, two bed-rest studies have shown no statistically significant changes in total body water (refs. 34 and 35). This finding raises the possibility that immobilization during bed rest is associated with an increase in intracellular fluid. However, no conclusive supporting data have been put forward to date; moreover, the findings conflict with spaceflight results (ref. 29).

U.S. Study

The changes in hormones and electrolytes seen in bed rest have not shown the magnitude of change observed in men returning from spaceflight. In recent years, greater and greater emphasis has been placed on head-down bed rest as a more accurate analog for weightlessness exposure. Clinical laboratory studies in the joint U.S./U.S.S.R. investigations were focused on comparing biochemical, hormonal, and hematologic changes in horizontal and head-down bed-rest subjects.

Urine samples were collected throughout the study and were pooled every 24 hr for analysis. Fasting blood samples (8-hr fast) were obtained by venipuncture from all subjects after they had spent 30 min in the supine position. Samples were collected between 0700 and 0800, except on recovery days 0 and 10, when they were collected in the afternoon following cardiovascular testing. (One unscheduled sample was obtained from one subject for white cell count and differential.) A complete listing of all tests conducted and methods of procedure are given in table 33. Blood sampling schedules are shown in figure 1.

All subjects were administered a water-load test in the fasting condition on day 9 of the control period and on the second day of recovery. For this test, the subjects drank distilled water equal to 2% of their body weight. The tests were conducted in the morning following blood sampling. Urine samples were collected 30 to 60 min before the test and at 30, 60, 90, 120, 180, and 240 min after water loading. Samples were analyzed for creatinine,

sodium, potassium, calcium, osmolality, aldosterone, and ADH. Blood samples (4 ml) were taken immediately before water loading and again 90 min afterward. The samples were analyzed for hemoglobin, sodium, potassium, calcium, osmolality, aldosterone, ADH, and pH. All subjects continued to fast until after the test was completed.

Radioisotope studies—Radioisotope measurements were used to evaluate red cell mass, hematocrit, and extracellular fluid. The radioisotopes used were ^{125}I human serum albumin (25 μCi), ^{35}S sulfate (25 μCi), and ^3H water (25 μCi). Before administration, each dose was diluted by saline to exactly 1 ml in volume.

Red cell mass, plasma volume, and extracellular fluid were determined by the following procedure. Blood (12.5 ml) was drawn into a special anticoagulant solution (2.5 ml of acid citrate dextrose) contained in a 20-ml syringe. An $\text{Na}_2^{51}\text{CrO}_4$ solution (37.5 μCi) was next injected into the syringe, and the contents were mixed slowly and continuously for 4 min. Ascorbic acid (50 mg) was then injected into the syringe, and the contents were again well mixed. Immediately thereafter, 10 ml of the tagged blood (25 $\mu\text{Ci}^{51}\text{Cr}$) were reinjected into the subject through the catheter-stopcock system, with the injection syringe washed with saline solution until no blood remained. The ^{51}Cr -tagged blood that was not reinjected was used as the subject's standard. A dose of ^{125}I albumin was next injected and the syringe washed with normal saline. The procedure used to inject the subjects was used in preparing standard dilutions for each determination so that they would duplicate each other exactly. Subjects were also given $^{35}\text{SO}_4$ and $^3\text{H}_2\text{O}$ orally. Red cell mass and plasma volume values were determined on the basis of a 30-min blood sample. Extracellular fluid values were determined by calculating the zero-time intercept using the least-squares method and the ^{35}S content of the samples at 30, 60, 90, and 120 min.

Duplicate microhematocrits were performed on all samples (4-min centrifugation). Blood samples were used for determining red cell mass were well mixed, and 0.2-ml aliquots were pipetted into triplicate sample tubes. Those for determining plasma volume also consisted of 0.2-ml aliquots pipetted into triplicate sample tubes. The ^{51}Cr standards were treated similarly. The ^{125}I albumin standards were made by diluting 1 ml of stock solution to 1 liter and pipetting 0.2-ml aliquots into sample tubes.

Sulfate space was determined by precipitating the plasma protein contained in 0.2 ml of plasma with 0.4 ml of Thanol. Duplicate aliquots (0.2 ml) of the supernatant were pipetted into an Aquasol counting solution (15 ml). The standard was obtained by adding 1 ml of $^{35}\text{SO}_4$ to a 25-ml volumetric flask with normal stock plasma. From this, 0.2-ml aliquots were treated in the same way as unknown plasmas.

TABLE 33.- LABORATORY ANALYSES AND PROCEDURES

Assay	Units	Sample	Procedure ^a
Hematology			
RBC	$10^{12}/l$	WB	Electronic
RETIC	%	WB	Microscopic-new methylene blue N
RETIC NO.	$10^9/l$	WB	Calculation: $\text{retic \%} \times \text{RBC}(10^{12}/l) \times 10^3$
RPI		WB	Calculation: $\frac{\text{retic \%} \times \text{Hct}(l/l) \times K}{45} \times 100$
HB	g/dl	WB	Spectrophotometric-cyanmethemoglobin
HCT	l/l	WB	Microhematocrit-centrifugation
MCV	fl	WB	Calculation: $\frac{\text{Hct}(l/l)}{\text{RBC}(10^{12}/l)} \times 1000$
MCH	pg	WB	Calculation: $\frac{\text{Hb}(g/dl)}{\text{RBC}(10^{12}/l)} \times 10$
MCHC	g/dl	WB	Calculation: $\frac{\text{Hb}(g/dl)}{\text{Hct}(l/l)} \times 1000$
ZSR	ml/ml	WB	Centrifugation and calc: $\frac{\text{Hct}(l/l)}{\text{Zetacrit}(\%)} \times 10,000$
RBC MORPH		WB	Microscopic: light and scanning electron microscope
PLAT	$10^9/l$	WB	Electronic; coincidence corrected + K_{Hct}
WBC	$10^9/l$	WB	Electronic
DIFF PCT	%	WB	Microscopic: Wright's stain
DIFF NO.	$10^9/l$	WB	Calculation: $\% \times \text{WBC}$
WBC MORPH		WB	Microscopic: Wright's stain
Special hematology			
RCM	ml	WB	Isotope dilution: ^{51}Cr
P VOL	ml	HP	Isotope: ^{125}I -albumin
BLD VOL	ml	WB	Calculation: $\text{RCM} + \text{P Vol}$
ESA	mg/dl	S	TC: mouse fetal liver; ^{59}Fe incorporation
FERRITIN	ng/ml	S	RIA: ^{59}Fe incorporation
HB ELECTROPHORESIS ^b	%	WB	Electrophoresis: Titan III cellulose acetate
A1, A2, F, S			
HB AIC	%	WB	Cation exchange column
TRANSFERRIN	mg/dl	S	EID: cellulose acetate-specific antiserum
HAPTOGLOBIN	mg/dl	S	EID: cellulose acetate-specific antiserum
HEMOPEXIN	mg/dl	S	RID: Mancini technique
CERULOPLASMIN	mg/dl	S	EID: cellulose acetate-specific antiserum
2,3-DPG	$\mu\text{mol/gHb}$	S	Enzymatic: Nygaard and Rorth
RETIC PROFILE	%	WB	Quantitative microphotometry ^c

TABLE 33.— CONTINUED

Assay	Units	Sample	Procedure ^a
Serology-immunology			
HBsAG ^b	Pos/neg	S	RIA: ausria II- ¹²⁵ I, Rel/CPM
CRP	Pos/neg	S	Polystyrene latex agglutination/If pos, RID
RPR ^b	Pos/neg	S	Flocculation: cardiolipin-cholesterol reagin
IGG	mg/dl	S	EID: cellulose acetate-specific antiserum
IGA	mg/dl	S	EID: cellulose acetate-specific antiserum
IGM	mg/dl	S	RID: buffered agarose gel with monospecific antibody
IGD	mg/dl	S	RID: buffered agarose gel with monospecific antibody
C3	mg/dl	S	RID: buffered agarose gel with monospecific antibody
C4	mg/dl	S	RID: buffered agarose gel with monospecific antibody
Cellular immunology			
Lymphocyte profile	%- 10 ⁸ /l	HWB	Electronic, E. Rosette, surface immunoglobulin, Isotope Incorp.
Chemistry: blood			
Glucose	mg/dl	S	Coupled enzymatic-hexokinase and glucose-6-phosphate dehydrogenase; mod. Barthelmai and Czak
Cholesterol	mg/dl	S	Enzymatic utilizing cholesterol esterase and cholesterol oxidase; Allain
AST	IU/l	S	UV-kinetic Wroblewski and Mod. Henry
ALT	IU/l	S	UV-kinetic Wroblewski and LaDue
BUN	mg/dl	S	Enzymatic with urease and glutamic dehydrogenase; mod. Talke and Schubert
Uric Acid	mg/dl	S	Hawk—reduction of phosphotungstate in the presence of cyanide
Alk Phos	IU/l	S	Kinetic using p-nitrophenyl phosphate; mod. Bessey et al.
CA	mg/dl	S	Willis—atomic absorption spectrophotometry
Mg	mg/dl	S	Willis—atomic absorption spectrophotometry
PO ₄	mg/dl	S	Fiske and Subbarow—dialyzed; phosphomolybdate—reduced by 1-amino-2-naphthol 4-sulfonic acid
Bili T	mg/dl	S	Formation of azobilirubin after reaction with diazotized sulfanilic acid; Jendrassik
Bili D	mg/dl	S	Reaction with diazo in acidic aqueous medium O-1N HCl; Jendrassik
Creat	mg/dl	S	Alkaline picrate (dialysis); Jaffe
CK	IU/l	S	Kinetic-coupled enzymatic of creatine phosphate to form NADH in the presence of glucose-6-phosphate dehydro-genase; mod. Oliver and Rosalki
LDH	IU/l	S	UV—kinetic using lactate to pyruvate; mod. Wacker
OSMOL	mOsm/kg	S	Freezing point depression
Na	mEq/l	S	Flame emission photometry
K	mEq/l	S	Flame emission photometry
Amylase	IU/l	S	UV—kinetic Mod. Henry and Chiamori
Cl	mEq/l	S	Amperometric titration with silver ions
Trigly	mg/dl	S	Enzymatic: Bucolo and David
GGTP	IU/l	S	Kinetic-utilizing glycylglycine; mod. Szasz

TABLE 33.—CONTINUED

Assay	Units	Sample	Procedure ^a
Special chemistry			
VLDL ^b	mg/dl	S	Calculation
LDL ^b	mg/dl	S	Calculation
HDL ^b	mg/dl	S	Extraction/enzymatic
Protein	g/dl	S	Refractometry
Alb	g/dl	S	Electrophoresis cellulose acetate with barbital buffer
Al	g/dl	S	Electrophoresis cellulose acetate with barbital buffer
A2	g/dl	S	Electrophoresis cellulose acetate with barbital buffer
B	g/dl	S	Electrophoresis cellulose acetate with barbital buffer
Gamma	g/dl	S	Electrophoresis cellulose acetate with barbital buffer
Lipo 1A	%	S	Electrophoresis cellulose acetate with barbital buffer
Lipo Pre Beta	%	S	Electrophoresis cellulose acetate with barbital buffer
Lipo Beta	%	S	Electrophoresis cellulose acetate with barbital buffer
LDH ISO 1-5	%	S	Electrophoresis cellulose acetate with barbital buffer
CK ISO	%	S	Electrophoresis UV fluorescent (cellulose acetate)
pH	—	HP	pH electrode
pCO ₂	mmHg	HP	pCO ₂ electrode
pO ₂	mmHg	HP	pO ₂ electrode
TCO ₂	mmol/l	HWB	Calculation Siggaard-Andersen alignment nomogram
Base Excess	mmol/l	HWB	Calculation Siggaard-Andersen alignment nomogram
Standard Bicarbonate	mmol/l	HWB	Calculation Siggaard-Andersen alignment nomogram
TBW	ml	Urine	³ HOH radioisotopic dilution
ECF	ml	HP	³⁵ SO ₄ radioisotopic dilution
Endocrinology: blood			
T-3	ng/dl	S	¹²⁵ I RIA solid phase
T-4	μg/dl	S	¹²⁵ I RIA solid phase
TSH	μIU/ml	S	¹²⁵ I RIA double antibody; solid phase
PTH	ng/ml	EP/HP	¹²⁵ I RIA single antibody; charcoal separation
CAL	ng/ml	EP/HP	¹²⁵ I RIA single antibody; dioxane separation
EPI	pg/ml	HP	³ H Radioenzymatic with TLC separation
NOREPI	pg/ml	HP	³ H Radioenzymatic with TLC separation
DA	pg/ml	HP	³ H Radioenzymatic with TLC separation
ANGIO I	ng/ml/hr	EP	¹²⁵ I RIA single antibody charcoal separation physiological pH
ALDO	pg/ml	EP	³ H RIA with methylene chloride; single antibody charcoal separation
ACTH	pg/ml	EP	¹²⁵ I RIA single antibody; charcoal separation
CORT	μg/dl	EP	¹²⁵ I RIA single antibody; solid phase
INS	μIU/l	EP	¹²⁵ I RIA double antibody; sandwich mechanism
HGH	ng/ml	EP	¹²⁵ I RIA double antibody
TESTO	μg/dl	EP	¹²⁵ I RIA ether extraction; double antibody
25-OH VIT D	ng/ml	HP/EP/S	¹²⁵ I CPB; charcoal separation
1,25 (OH) ₂ VIT D	pg/ml	HP	HPLC/protein binding
VIT B12	pg/ml	S	⁵⁷ Co CPB; charcoal separation
FOLATE	ng/ml	S	¹²⁵ I CPB charcoal separation
DBH	nm/ml/hr	S/HP	¹⁴ C Radioenzymatic PNNT-enzyme
ADH	pg/ml	HP/EP	¹²⁵ I RIA-double antibody

TABLE 33.- CONCLUDED

Assay	Units	Sample	Procedure ^a
Routine urinalysis			
Nitrite	pos/neg	urine	3 Hydroxy-1,2,3,4-tetrohydro-7,8 benzoquinoline
pH		urine	Bromthymol blue
Prot	neg-3+	urine	Tetrachlorophenol
Glu	neg-3+	urine	Glucose oxidase
Keto	neg-3+	urine	Sodium nitroferricyanide
Urobilin	normal- 12 mg/dl	urine	4-methoxybenzene-diazoniumtetrafluoroborate
Bili	neg-3+	urine	2,6 Dichlorobenzene
Blood	neg-about 250 Ery/ μ l	urine	O-toluidine
WBC	cells/hpf	urine	Microscopy
RBC	cells/hpf	urine	Microscopy
Epith	cells/hpf	urine	Microscopy
Mucous	-	urine	Microscopy
Casts	No./hpf	urine	Microscopy
Color	-	urine	Visual inspection
Appearance	-	urine	Visual inspection
Chemistry: urine			
Volume	ml	urine-24 hr or random	Volumetric
Specific Gravity	-	urine	Refractometry
Osmolarity	mOsm	urine	Freezing point depression
Protein	mg	urine	Refractometry
Na	mEq/Vol	urine	Flame emission photometry
K	mEq/Vol	urine	Flame emission photometry
Cl	mEq/Vol	urine	Amperometric titration
Ca	mEq/Vol	urine	Atomic absorption
Mg	mEq/Vol	urine	Atomic absorption
IPO ₄	mg/Vol	urine	Phosphomolybdate
Uric Acid	mg/Vol	urine	Phosphotungstate with cyanide
Creat	mg/Vol	urine	Alkaline picrate
Endocrinology: urine			
ALDO	μ g/TV	urine	³ H RIA acid hydrolysis extraction with methylene chloride
CORT	μ g/TV	urine	¹²⁵ I RIA methylene chloride extraction; single antibody; solid phase
TESTO	μ g/TV	urine	¹²⁵ I RIA ether extraction; glucuronidase hydrolysis; double antibody
TOT EPI	μ g/TV	urine	Acid hydrolysis, open column chromatography, fluorometric
TOT NOREPI	μ g/TV	urine	Acid hydrolysis, open column chromatography, fluorometric
ADH	mIU/TV	urine	Open column chromatography, ¹²⁵ I RIA single antibody, charcoal separation

Abbreviations: EID = electroimmunodiffusion; EP = EDTA plasma; FP = sodium fluoride plasma; HP = heparin plasma; HWB = heparinized whole blood; RIA = radioimmunoassay; RID = radioimmunodiffusion; S = serum; TC = tissue culture; WB = whole blood.

^aNumbers in parentheses refer to sources as they are cited in reference 37 of this report.

^bSelection examination only.

^cMethylene blue and 1-ethyl-2[3-(1-ethylnaphtho[1,2d]-thiazolin-2-ylidene)-2-methyl-propenyl]naphtho[1,2d]-thiazolium bromide.

Radioactive studies of total body water used the $^3\text{H}_2\text{O}$ content of background urine and three spot urines collected 3 to 8 hr after dosage. Each subject emptied his bladder at least once between the injections of $^3\text{H}_2\text{O}$ and the emptying of the spot urines. Urine samples were distilled, and the distillate (0.5 ml) was pipetted into an Aquasol counting solution (15 ml). The body-water standard was achieved by diluting 1 ml of the stock solution to 1 liter and pipetting, in triplicate, 0.5-ml aliquots into 15 ml of Aquasol.

Radioactivity was monitored by measuring beta radioactivity in a liquid scintillation counter and gamma radioactivity in a scintillation well counter. In both measurements, multiple counts were obtained until a 1% counting error was achieved. Subjects received total radioactive doses of 0.0432 rem, which compares favorably with the total permissible occupational exposure of 1.25 rem/quarter, which can be increased to 3.0 rem/quarter if the total for the year is less than 5.0 rem.

Cellular immunology— Cellular immunological responses were studied in both groups of subjects, with tests made 3 days before bed rest, on the seventh day of bed rest, and on the first day of recovery. Tests were conducted for white blood cell count; lymphocyte count, T cell, B cell, and null cell distributions; and lymphocytic responsiveness to the mitogens PHA, Con A, and pokeweed. Before assay, the samples were stored for 24 hr to lower the total white blood cell count resulting from cell death, which would affect primarily the neutrophils.

Results of biochemical and endocrine analyses— Selected 24-hr-mean urinary and serum biochemical and endocrine results are shown in tables 34 and 35. These include parameters from the full list of analyses (see table 33) showing evidence of significant ($p < 0.05$) or near-significant change compared to control (pre-bed-rest) levels. Data for all parameters (table 33) are given in the original reports submitted for this experiment. Both the horizontal and head-down subjects exhibited decreased excretion of sodium, chloride, and potassium during the bed-rest and recovery periods relative to the baseline values. But osmolality and specific gravity measurements indicated a more concentrated urine in both groups. There also was a significant decrease in 24-hr-urine volume between the control period and bed rest or recovery (fig. 8). During bed rest, urinary aldosterone increased slightly in the horizontal group, but decreased in the head-down group. During recovery, both groups showed increased aldosterone. Antidiuretic hormone, on the other

hand, was slightly increased in both groups during bed rest, except for the head-down group on the first day of bed rest, when it was lowered. In the recovery period, both groups showed slight increases in ADH.

Urine creatinine findings (table 34) were variable but, in general, were slightly increased in both groups during bed rest. Epinephrine and norepinephrine were decreased in both groups during the bed-rest period; during recovery, there was a tendency for these substances to increase back toward the bed rest levels. Testosterone was generally decreased in both groups. Findings for calcium and inorganic phosphate excretion were variable, but urinary levels of these parameters generally increased during bed rest in both groups. Findings on magnesium excretion were more consistent, with this electrolyte decreasing during bed rest and tending to increase during recovery in both groups.

Plasma and serum biochemistry and endocrine results (table 35) indicated that both groups experienced losses in sodium, potassium, chloride, osmolality, cortisol, and aldosterone concentrations during bed rest; sodium, potassium, chlorine, glucose, cholesterol, osmolality, and insulin were depressed in the recovery period. Aldosterone, which had decreased during bed rest, actually increased during recovery. Serum norepinephrine increased in the head-down group during bed rest and increased in both groups following bed rest; but epinephrine and dopamine beta hydroxylase (DBH) were more variable. Plasma ADH tended to decrease in both groups, except in the head-down group on the fourth day of recovery. In both groups, PTH was decreased on day 2 of bed rest, but increased on day 4. Both $1,25(\text{OH})_2$ and 25-OHD were decreased during bed rest, but returned to baseline values or higher after recovery. There were general increases in AST and ALT during bed rest and upon recovery. Both groups exhibited increases in alkaline phosphatase and LDH early in bed rest, with the horizontal group showing an increase in LDH isoenzyme on day 7 of recovery. Uric acid (table 35) was decreased in the horizontal subjects throughout bed rest and slightly increased in the head-down subjects on day 2 of bed rest. There was a significant difference in serum uric acid levels between horizontal and head-down groups, uric acid being lower in the latter subjects. Again, in both groups, HGH and T_3 were decreased following bed rest, T_4 was slightly increased during the recovery period, and thyroid stimulating hormone (TSH) showed no consistent changes.

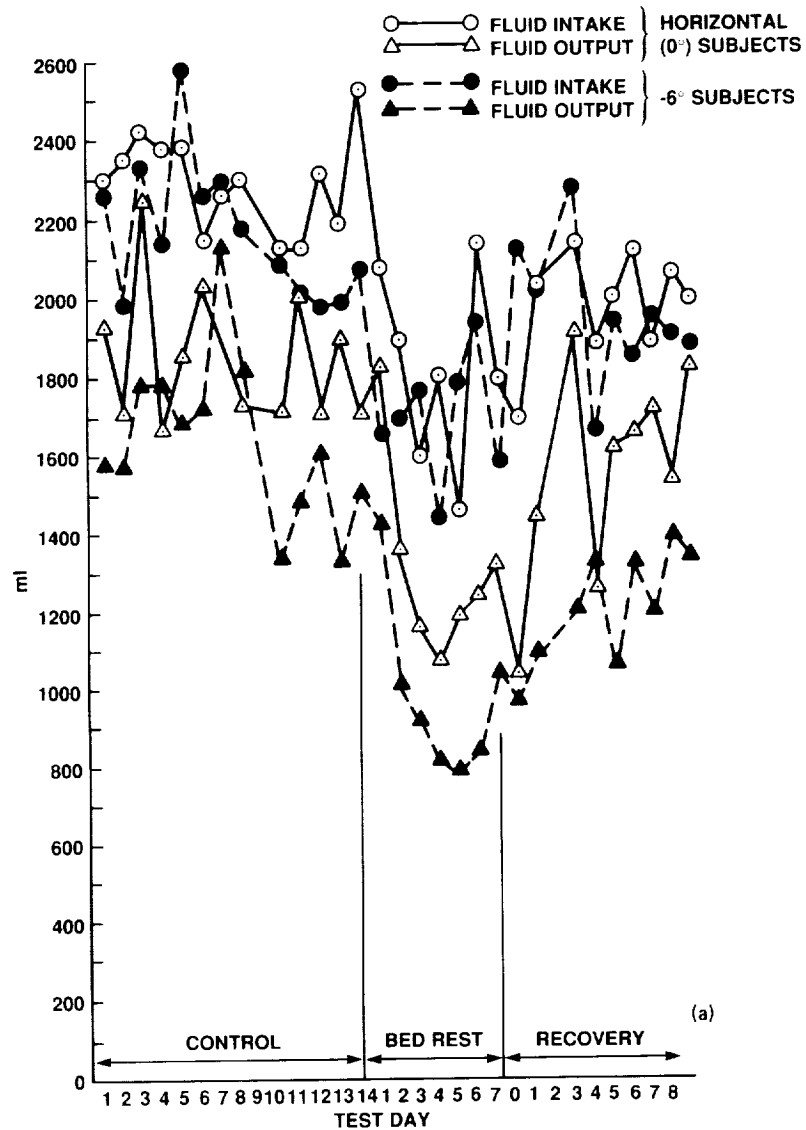


Figure 8.— Mean fluid balance: U.S. subjects. (a) Fluid intake, fluid output.

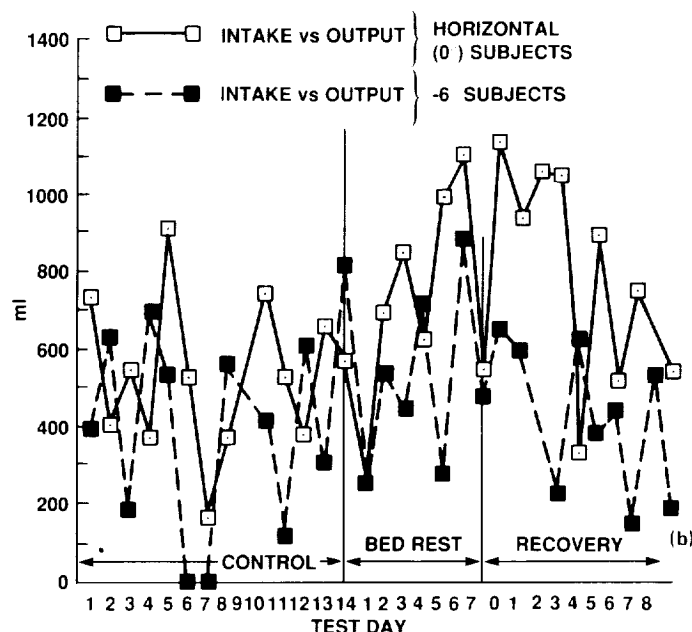


Figure 8.— Concluded. (b) Intake versus output.

Discussion— Exposure to weightlessness results in a redistribution of the volume of blood within the vascular system. The body sensors interpret this redistribution to be an increase in blood volume and respond by causing a compensatory loss in water, sodium, and potassium from the renal tubules. Following spaceflight, both astronauts and cosmonauts have shown a loss in body weight which is rapidly regained. Most of this loss is attributed to water loss; the remainder is thought to consist of fat, protein (muscle), and bone. The decreased adiposity has been attributed to a hypocaloric diet eaten during flight (loss of appetite) and to muscle loss caused by inactivity or lack of gravitational force, or both.

Fluid balance findings are shown in figure 8 for the U.S., which compares water intake, urine output, and resulting balance. A frank diuresis was not evident on the first day of bed rest. This was also the case for the U.S.S.R. subjects (see fig. 9). The findings may have been a result of the fact that the subjects were fed standard spaceflight diets instead of more usual table food. In both horizontal and head-down groups, urine excreted during bed rest was more concentrated and of less volume. On the first day of bed rest, excreted ADH increased slightly in the horizontal group and decreased in the head-down subjects; throughout the remainder of bed rest, it was generally increased in both groups. Thus, after the initial adjustment to bed rest, the subjects in this study apparently were in a water-conserving state, which occurred on the first day of bed rest in the horizontal subjects, but required 2 days in the head-down group. Intake-output data from the present study, in general,

agree with reports from spaceflights, during which an early diuresis has not been a regular finding.

Serum sodium concentration decreased similarly in both groups, both in timing and magnitude of change. Serum potassium also decreased in both groups, but was statistically significant only in the head-down subjects, even though both groups had ingested like amounts of supplemental potassiums.

Plasma angiotensin I was slightly increased late in bed rest and more so during recovery in both groups. Plasma aldosterone, on the other hand, decreased during bed rest, but increased during recovery in both groups. Urinary aldosterone increased during bed rest in the horizontal group, but not in the head-down group; however, both groups exhibited increases during recovery. The results suggest that the renin-angiotensin-aldosterone mechanism for conserving sodium occurred only in the horizontal subjects. The increase, however, was not as great as that usually reported early in spaceflight, and there was no evidence to suggest that the head-down position augmented the aldosterone response.

Other investigators have observed a decrease in plasma angiotensin I, aldosterone, and ADH in head-down subjects on the first day of bed rest (ref. 36). These findings suggest that head-down subjects exhibit a rapid physiological response when placed in this position, leading to hemodynamic and neurohumoral adaptation, which includes shifts in water-salt volume to produce a reduced blood volume. In the present study, plasma values were not obtained on the first day of bed rest, but urine levels

TABLE 34.- 24-HOUR URINE: U.S. STUDY

MOSM	Mean control	Bed rest				Recovery			
		Day 1	Day 2	Day 5	Day 7	Day 0	Day 1	Day 3	
mOsm									
0°	551 ±11	588 ±19	772 ± 52 ^a	816 ±41 ^a	656 ±58	805 ±38 ^a	659 ±69	456 ±31 ^a	
-6°	637 ±16	700 ±71	857 ±100	963 ±81 ^a	769 ±131	780 ±136	697 ±79	653 ±26	
Na, mEq/TV									
0°	200 ±4	224 ±14	208 ±15	169 ±15	141 ±27	113 ±17 ^a	142 ±19 ^a	178 ±18	
-6°	189 ±5	207 ±16	133 ±12 ^a	117 ±10 ^a	116 ±10 ^a	86 ±12 ^a	105 ±24 ^a	147 ±23	
K, mEq/TV									
0°	73 ±1	79 ±6	74 ±8	81 ±8	67 ±9	65 ±5	63 ±4	62 ±6	
-6°	61 ±2	58 ±4	63 ±5	55 ±6	53 ±6	51 ±4	45 ±9	60 ±9	
Cl, mEq/TV									
0°	184 ±4	195 ±14	186 ±9	138 ±17 ^a	116 ±23 ^a	84 ±12 ^a	111 ±17 ^a	158 ±12	
-6°	175 ±5	187 ±13	150 ±11	107 ±14 ^a	102 ±14 ^a	78 ±12 ^a	93 ±21 ^a	138 ±19	
Ca, mg/TV									
0°	11.3 ±0.2	11.5 ±1.1	12.8 ±0.5 ^a	12.1 ±0.9	10.5 ±1.1	11.6 ±0.8	11.4 ±0.5	11.9 ±0.6	
-6°	13.7 ±0.2	14.3 ±0.2	15.2 ±0.9	14.9 ±1.6	12.7 ±1.2	14.7 ±1	12.5 ±1.2	11.9 ±1.6	
Creat., mg/TV									
0°	1.64 ±0.02	1.67 ±0.02	1.71 ±0.02	1.75 ±0.10	1.73 ±0.09	1.78 ±0.07	1.82 ±0.07	1.72 ±0.11	
-6°	1.66 ±0.02	1.67 ±0.06	1.65 ±0.10	1.72 ±0.08	1.86 ±0.06 ^a	1.82 ±0.06 ^a	1.71 ±0.06	1.64 ±0.09	
Aldo., µg/TV									
0°	12.7 ±0.5	12.5 ±3.2	15.6 ±2.7	17.2 ±2.1	15 ±1.7	21.2 ±1.9 ^a	18.3 ±2.9	13.1 ±1.1	
-6°	10.9 ±0.4	9.6 ±1.6	8.5 ±0.7 ^a	12.3 ±1.4	10.2 ±1.8	17.1 ±1.3 ^a	14.1 ±2.8	11.8 ±1	
Epi., µg/TV									
0°	18.9 ±1.5	10.8 ±3.6	7.1 ±1.7 ^a	7.2 ±2.6 ^a	10.9 ±2	11.8 ±4	15.6 ±4	15.7 ±2.6	
-6°	18.3 ±1.9	12.9 ±4.2	6.9 ±5.8	10.6 ±3.6	10.6 ±4.6	19.6 ±2.1	12.7 ±1.6 ^a	10.5 ±3.4	
Norepi., µg/TV									
0°	49.2 ±2.5	34.2 ±4.2 ^a	31.5 ±4.7 ^a	35.5 ±5.4	33.4 ±4.6 ^a	44.8 ±5.3	44 ±4.7	48 ±7.7	
-6°	48.5 ±2.7	31.3 ±7.3	32.4 ±3.5	31.4 ±6.5	32.6 ±4.1 ^a	33.7 ±5.9	34.2 ±2.8 ^a	42 ±4.2	

^ap < 0.05 compared to control period.

TABLE 35.—SERUM, BIOCHEMICAL, AND ENDOCRINE DATA: U.S. STUDY

Mean \pm SE	Mean control	Bed rest			Recovery		
		Day 2	Day 4	Day 7	Day 2	Day 7	
Na, mEq/l							
0°	140 \pm 1	138 \pm 1	135 \pm 1	138 \pm 1	139 \pm 1	141 \pm 1	
-6°	140 \pm 1	138 \pm 1	135 \pm 1	137 \pm 1	137 \pm 1	139 \pm 1	
K, mEq/l							
0°	4 \pm 0.03	4 \pm 0.1	3.9 \pm 0.01	3.9 \pm 0.01	3.8 \pm 0.1	3.8 \pm 0.1	
-6°	4.2 \pm 0.1	4.1 \pm 0.1	3.9 \pm 0.01 ^a	3.7 \pm 0.01 ^a	3.7 \pm 0.01 ^a	4.1 \pm 0.2	
Cl, mEq/l							
0°	100 \pm 0.4	97 \pm 1 ^a	98 \pm 0.3 ^a	98 \pm 1 ^a	99 \pm 1 ^a	98 \pm 1	
-6°	100 \pm 0.4	99 \pm 1	99 \pm 1 ^a	99 \pm 1	98 \pm 1 ^a	98 \pm 1	
mOsm							
0°	274 \pm 1	273 \pm 3	269 \pm 2	270 \pm 2	270 \pm 1 ^a	268 \pm 1	
-6°	286 \pm 1	281 \pm 2	282 \pm 2	281 \pm 3	284 \pm 2	278 \pm 3	
Ca, mg/dl							
0°	9.2 \pm 0.1	10.2 \pm 0.2 ^a	—	9.5 \pm 0.1	9.3 \pm 0.2	9.7 \pm 0.1	
-6°	9.1 \pm 0.1	10.2 \pm 0.1 ^a	—	9.3 \pm 0.1	9.1 \pm 0.1	9.7 \pm 0.1	
Aldo, pg/ml							
0°	335 \pm 24	223 \pm 18 ^a	232 \pm 18 ^a	273 \pm 22 ^a	475 \pm 75	366 \pm 20	
-6°	325 \pm 26	228 \pm 37 ^a	258 \pm 23 ^a	233 \pm 36 ^a	350 \pm 98	294 \pm 17	
Cortisol, μ %							
0°	19.2 \pm 0.6	17.6 \pm 2.2	17.2 \pm 1.5	19 \pm 1.4	23.3 \pm 2.7	15.4 \pm 1.5	
-6°	19 \pm 0.9	17.9 \pm 0.2 ^a	20.2 \pm 1.2	18.8 \pm 1.1	18.9 \pm 1.2	15.5 \pm 1.1	
Angio I, ng/ml/hr							
0°	2.33 \pm 0.28	2.33 \pm 0.43	2.91 \pm 0.62	4.02 \pm 1.1	10.98 \pm 5	2.91 \pm 1.05	
-6°	1.92 \pm 0.12	2.75 \pm 0.5	3.13 \pm 0.9	4.10 \pm 0.8	6.20 \pm 1.1	3.85 \pm 1.02	
Epi, pg/ml							
0°	19 \pm 6	15 \pm 5	24 \pm 9	16 \pm 15	32 \pm 7	18 \pm 11	
-6°	29 \pm 8	16 \pm 13	41 \pm 23	18 \pm 8	25 \pm 6	35 \pm 22	
Norepi, pg/ml							
0°	244 \pm 35	224 \pm 8	244 \pm 22	241 \pm 24	251 \pm 14	244 \pm 15	
-6°	274 \pm 30	345 \pm 38	340 \pm 48	325 \pm 45	391 \pm 35 ^a	294 \pm 34	
Glucose, mg/dl							
0°	87 \pm 1	88 \pm 2	90 \pm 3	81 \pm 4	78 \pm 3 ^a	81 \pm 2	
-6°	84 \pm 1	87 \pm 2	85 \pm 2	87 \pm 5	74 \pm 2 ^a	80 \pm 1	
Insulin, μ IU/l							
0°	26 \pm 2	23 \pm 1 ^a	27 \pm 6	30 \pm 9	24 \pm 4	19 \pm 3	
-6°	22 \pm 2	19 \pm 2	20 \pm 4	19 \pm 2	21 \pm 5	15 \pm 2	
Chol, mg/dl							
0°	236 \pm 9	259 \pm 4	267 \pm 1 ^a	241 \pm 7	219 \pm 7	214 \pm 6	
-6°	193 \pm 2	212 \pm 5 ^a	221 \pm 8 ^a	200 \pm 8	175 \pm 5 ^a	178 \pm 6	
Uric Acid, mg/dl							
0°	6.9 \pm 0.1	6.4 \pm 0.1	—	6.2 \pm 0.2 ^a	6.3 \pm 0.2	6.3 \pm 0.2	
-6°	5.7 \pm 0.3	6.1 \pm 0.3	—	5.5 \pm 0.5	5.8 \pm 0.4	5.7 \pm 0.4	

^ap < 0.05 compared to control period.

of the hormones indicate that similar mechanisms operated in the head-down subjects. The increase in serum creatinine and slight increase in urinary creatinine, particularly in the head-down subjects, indicate a decrease in creatinine clearance which probably resulted from a change in blood flow to the kidneys. Creatinine clearance has also decreased slightly in some space crewmen (ref. 37).

The slight decreases in serum uric acid and slight increases in urinary uric acid may be attributed to altered ADH secretion or to changes in the renal handling of uric acid. Astronauts and cosmonauts have exhibited similar changes (ref. 38).

Responses of the adrenal cortex and medulla in this study are of particular interest. Urine epinephrine levels rose during bed rest, probably because of stress. Cortisol, the major glucocorticoid of the adrenal cortex, has been observed to increase in both spaceflight and bed rest (ref. 33). The present study, however, showed slight decreases in both plasma and urinary cortisol. But it should be noted that control-period plasma cortisol values were in the high normal range. The variable ACTH findings in the present study suggest that the pituitary-adrenal axis responded to bed-rest conditions. Plasma norepinephrine was increased in the head-down subjects throughout bed rest and in both groups with recovery. Dopamine increased in both groups with bed rest, but DBH increased only in the head-down subjects. Since DBH is responsible for hydroxylating dopamine to form norepinephrine (ref. 39), this enzyme should be elevated if there is a demand for norepinephrine production or release. The findings demonstrated a general responsiveness of the sympathetic nervous system to bed rest, particularly in the head-down subjects. Increases in the enzyme that occurred during the recovery period were similar to responses during and after spaceflight as a general response to stress and to maintain orthostatic control (refs. 1 and 33).

Resting plasma glucose has been reported to increase with bed rest (refs. 40 and 41). The subjects in the present study exhibited this response during bed rest, but showed significant decreases afterward. Insulin, on the other hand, was consistently lower than baseline values during both bed rest and recovery. Research has shown that bed-rested subjects have reduced tolerance to glucose, whether administered orally or intravenously. The cause of this change is not known. Such challenges with oral glucose loads were not conducted during the present study. The general decreases in growth hormone observed in the present study have been observed before with immobilization (ref. 41).

Findings in this study of increased cholesterol during bed rest and decreased cholesterol after bed rest are supported by previous research (ref. 42). Diet is not believed

to be responsible for this change, since the diet provided in this study was consistent in quality, if not in quantity, in all three study periods. Thyroid hormones were not measured in the joint study during bed rest, but in other research, thyroxine (T_4) has increased (ref. 43). The slight decrease in T_3 and increase in T_4 observed in the present study during recovery are consistent with blocked T_4 - T_3 conversion, which suggests that a change occurs in renal or liver handling of these substances.

Analysis for serum enzymes that might indicate altered liver, bone, and muscle functions failed to indicate significant changes. Although some individual readings were elevated, in general there were no significant changes in AST, ALT, LDH, CPK, and bilirubin. The slight increases in alkaline phosphatase seen in the horizontal group were similar to those observed after Apollo flights, but not after Skylab (refs. 37 and 44).

Findings of the present study indicate that musculoskeletal changes occurred with bed rest in both the horizontal and head-down subjects. This is supported by the slight decreases seen in CPK which have also been noted in other studies (ref. 45) and are thought to result from decreased muscle activity during bed rest. All of the change in CPK isoenzymes occurred in the MM band, indicating that only muscle CPK was involved. Although LDH isoenzyme patterns are useful in determining specific tissue changes, in this study neither group exhibited significant deviations from baseline values. In both groups, serum gamma-glutamyl transpeptidase activity was slightly elevated during bed rest and recovery. But these changes were small compared with changes evident during clinically apparent kidney and liver disorders. This enzyme is considered to play a role in protein biosynthesis and in the transport of amino acids across cellular membranes in kidney tubules (ref. 46). Changes in blood flow to the liver or kidneys may have been responsible for the slight elevation observed in the subjects.

An alteration in skeletal homeostasis was indicated by changes in serum calcium and inorganic phosphate which increased slightly and from 24-hr-urine calcium and phosphorus excretion, which also increased in both groups, with the magnitude of change being about the same in both. These changes occurred despite a general decrease in calcium (200 mg/day) in the diet. These findings are supported by previous bed-rest data (ref. 47), and by spaceflight findings of increased excretion of calcium and phosphorus (ref. 48).

Urinary testosterone increased in the horizontal subjects and decreased in the head-down group with bed rest, whereas plasma concentrations generally were decreased in both groups. These findings suggest that changes either in binding protein or in blood flow were responsible. With the Skylab mission, testosterone was increased during flight and decreased postflight. It is hypothesized that

these changes are caused by the same mechanisms that result in observed decreases in cortisol.

Shifts in fluids and electrolytes— During the present study, all subjects lost body weight (see table 24) and showed decreases in mean values of daily water intake and 24-hr-urine volumes and shifts in body-fluid compartments (see table 36 and fig. 8). These changes were most pronounced early in bed rest and during the recovery period.

Weight losses usually have not occurred with bed rest when caloric intake has been carefully maintained. But all subjects in this study lost weight on their Shuttle astronaut diet, with no difference between the horizontal and head-down subjects. Weight losses averaged about 0.45 kg and began on the first day of bed rest for the head-down subjects and on the second day of bed rest for the horizontal group; the losses probably resulted from a noticeable decrease in water and food intake during the bed-rest period. Water intake decreased by several hundred milliliters per day in the horizontal subjects and by about 1 liter/day in the head-down group, but the differences

were not statistically significant. Similarly, caloric intake decreased by several hundred calories per day in the horizontal group and by 1,000 kcal/day in the head-down subjects during bed rest. Although weight losses in the two groups did not differ, the difference in food intake was statistically significant.

Extracellular volume was measured 9 days before bed rest and on the last day (day 7) of bed rest. Changes in the horizontal and head-down groups were not significant, with decreases of 0.4% and 1.4%, respectively.

All horizontal and head-down subjects exhibited a decrease in red cell mass by the seventh day of bed rest, as shown in table 36. The mean decrease for the head-down group (–8.7%) did not differ significantly from that of the horizontal subjects (–5.5%). During the first 7 days of recovery, red cell mass continued to decrease in two subjects from each group. As expected, plasma volume decreased after 7 days of bed rest in both the horizontal and head-down subjects, but both had returned to baseline values by day 7 of recovery. No differences were seen between the responses of the two groups. Blood volume,

TABLE 36.— BODY FLUID VOLUME CHANGES WITH BED REST
[Mean \pm (SE)]

	Red cell mass, ml/kg	Plasma volume, ml/kg	Blood volume, ml	Extracellular fluid, ml/kg	Total body water, ml/kg
U.S. study					
Horizontal					
Control period	27.1 (2)	42.3 (2.6)	4732 (312)	203 (11)	599 (13)
Bed-rest day 7	25.8 (1.6) ^a	39.4 (2.2) ^a	4387 (255) ^a	204 (11)	596 (11)
Recovery day 7	25.2 (1.4) ^a	42.7 (2.8)	4586 (282)	—	—
Head-down					
Control period	26.1 (1.9)	40.2 (2.6)	4603 (300)	192 (6)	585 (18)
Bed-rest day 7	24.4 (1.8) ^a	37.9 (2.5) ^a	4230 (290) ^a	194 (6)	590 (18)
Recovery day 7	23.7 (1.9) ^a	41.0 (2.6)	4430 (306)	—	—
U.S.S.R. study					
Horizontal					
Control period	28.4 (1.1)	40.5 (1.5)	68.3 (2)	216 (8)	612 (9)
Bed-rest day 7	25.9 (0.8)	39.3 (1.7)	66.3 (3)	204 (13)	594 (8)
Recovery day 9	26.5 (1.2)	43.8 (1.9)	70.2 (3)	238 (19)	613 (14)
Head-down					
Control period	26.7 (0.9)	38.4 (1.2)	65.1 (1.9)	210 (8)	607 (14)
Bed-rest day 7	25.3 (0.7)	37.5 (0.7)	65.6 (1.7)	207 (7)	611 (13)
Recovery day 9	26.4 (1.4)	41.6 (1.2)	67.8 (2)	229 (7)	624 (17)

^ap > 0.05.

the combination of red cell mass and plasma volume, decreased after bed rest by 8.1% in the head-down group and by 7.1% in the horizontal group. After 7 days of upright activity, red cell mass remained depressed. Analyses of erythroid stimulating activity (ESA) indicate an elevation (compared to the control period) on recovery days 0 and 2, while there was no significant changes in ESA titers in either group during bed rest. A similar pattern was reported in previous 7-day bed-rest studies (ref. 33).

Water load test—Urine results with water loading are shown in table 37. As the data indicate, responses in the two groups were similar—by 2 hr after loading, 60% to 70% of the water load had been excreted. The most dilute urine was also voided during this time. Aldosterone was decreased until ADH responses occurred at 180 min. Plasma results obtained 30 min before and 90 min after loading are shown in table 38. The dilution effect of the water load was detected by osmolality measurements in the two groups. Sodium, aldosterone, and ADH were decreased at 90 min; potassium was slightly increased, except in the head-down subjects on day 2 of the recovery period. However, no significant differences were found between the two groups.

The water-load test was used to study the mechanisms that regulate excretion of water and sodium, particularly the hormonal system that controls such elimination. A healthy, normally hydrated individual usually excretes 60% or more of the water consumed over a 2-hr period and, in 4 hr, may excrete more than was consumed (ref. 49). It is believed that ingested water reduces the osmotic concentration of the extracellular fluid, so that secretion of ADH is suppressed and excretion of urine is increased. Results of the present study show that this mechanism was not impaired after 1 week of bed rest. U.S.S.R. postflight findings indicate that some crewmen are unable to excrete a water load rapidly after exposure to weightlessness. The adrenal system apparently was not involved in these latter tests, since there were no changes in urinary 17-oxycorticosteroids or in the potassium/sodium ratio. There were similar findings for all subjects in the present tests.

Hematology/immunology—Routine hematology results obtained during the U.S. study are shown in table 39. Hemoglobin increased significantly and hematocrit increased slightly and similarly in both groups during bed rest. Following bed rest, however, these variables decreased to or below bed-rest values in both groups. Following bed rest, both groups exhibited an increase in reticulocyte counts, with a shift to reticulocytes containing more ribosomal material.

Serum proteins—No significant changes were observed in total serum protein and its electrophoretic

pattern in either subject group over the course of the present study. Plasma albumin concentrations did not change significantly and are of note since they would have been expected to show increases of 10%-20% as compensatory changes associated with observed decreases in plasma volume. No significant changes were seen in immunoglobulin and other serum proteins examined, except for complement factor 3, which was elevated on recovery days 2 and 7 in both subject groups.

In cellular immunological studies, no significant changes were observed except for pokeweed mitogen stimulation of lymphocytes. Baseline values differed for the horizontal (9.7 index) and head-down (5.5 index) subjects; all were below an index of 10, which is considered to be low normal. As the study progressed, these values increased in all subjects to normal levels, suggesting that bed rest or confinement contributed to an initial decrease of response.

Discussion—Both spaceflight and bed rest produce a decrease in plasma volume. After 8 days in space, Gemini-5 crewmen exhibited losses in plasma volume of 9% and 5%. Previous bed-rest studies of 7- to 10-days' duration showed losses up to 10%, which have occurred during the first 48 hr of exposure (refs. 2 and 50). Both the horizontal and head-down subjects showed a loss of 8%, which is similar to previous findings for spaceflight and bed rest.

Losses in red cell mass were significantly smaller in the horizontal subjects (-6%) and head-down subjects (-9%) in the present study than in the two Gemini-5 crewmen (-20% and -22%). The loss in red cell mass in those crewmen was attributed to the hyperoxic atmosphere of the Gemini spacecraft. In early Apollo missions, on the other hand, red cell mass decreases were similar to those seen with bed rest (-22% to -7%), although later missions showed larger losses in red cell mass (-10%) (ref. 51). The losses in the subjects in the present study, however, were greater than have been noted in other bed-rest studies (usually -2% to -3%) with similar procedures. The reasons for this change are unclear. In the present study, hematocrit and serum protein concentration did not show significant changes as the result of bed rest. It is thought that the restricted physical activity imposed on the subjects during the 14-day control period may have contributed to this finding in that baseline values taken late in the control period may have already been reduced in level. The large decrease seen in red cell mass in the subjects would also tend to neutralize any hemoconcentration caused by a decrease in plasma volume.

In summary, the hematologic/immunologic bed-rest findings of the present study were similar to those seen previously in studies of similar length and characteristics, with similar changes observed in both groups.

TABLE 37.- URINE RESULTS, WATER LOAD TEST: U.S. STUDY

Time from water load, min	Volume		Na		K		Ca		ADH		Aldo.		Creat.		Osmo.
	ml	%	mEq/V	%	mEq/V	%	mg/V	%	μ U/V	%	μ g/V	%	mg/V	%	mOsmo
Horizontal subjects															
Control-day 7															
30	54 \pm 16	4	2 \pm 0.8	24	4 \pm 0.6	17	0.3 \pm 0.07	35	0.6 \pm 0.18	43	0.7 \pm 0.12	19	54 \pm 4	21	13 \pm 1
60	187 \pm 37	17	2 \pm 0.4	35	3 \pm 0.3	30	0.1 \pm 0.02	49	0.1 \pm 0.04	50	0.5 \pm 0.07	34	41 \pm 4	37	9 \pm 1
90	299 \pm 49	37	3 \pm 0.6	45	3 \pm 0.4	42	0.1 \pm 0.02	57	0.1 \pm 0.04	57	0.3 \pm 0.06	43	32 \pm 3	49	7 \pm 1
120	292 \pm 62	58	3 \pm 0.7	55	4 \pm 0.4	58	0.1 \pm 0.01	68	0.1 \pm 0.05	64	0.3 \pm 0.02	53	32 \pm 3	62	9 \pm 1
180	393 \pm 66	85	5 \pm 1.3	74	5 \pm 0.7	80	0.1 \pm 0.05	83	0.2 \pm 0.04	79	0.6 \pm 0.09	68	53 \pm 1	82	15 \pm 2
240	223 \pm 44	100	7 \pm 2.6	100	5 \pm 0.7	100	0.1 \pm 0.03	100	0.3 \pm 0.06	100	1.2 \pm 0.49	100	46 \pm 3	100	14 \pm 2
R + 2															
30	67 \pm 9	5	6 \pm 0.8	24	3 \pm 0.4	18	0.5 \pm 0.06	32	0.6 \pm 0.11	35	1.2 \pm 0.20	37	31 \pm 6	24	14 \pm 2
60	167 \pm 34	17	3 \pm 0.6	32	2 \pm 0.6	28	0.2 \pm 0.04	44	0.1 \pm 0.05	41	0.3 \pm 0.10	37	64 \pm 26	45	9 \pm 2
90	332 \pm 53	40	3 \pm 0.9	43	3 \pm 0.9	43	0.2 \pm 0.04	56	0.1 \pm 0.07	47	0.4 \pm 0.15	48	38 \pm 4	58	9 \pm 1
120	328 \pm 41	64	2 \pm 0.8	49	2 \pm 0.7	56	0.1 \pm 0.04	65	0.1 \pm 0.08	53	0.2 \pm 0.05	61	34 \pm 4	70	8 \pm 1
180	358 \pm 65	89	5 \pm 1	69	4 \pm 1	79	0.2 \pm 0.07	82	0.3 \pm 0.22	71	0.4 \pm 0.11	82	47 \pm 7	85	24 \pm 12
240	152 \pm 51	100	8 \pm 2.1	100	4 \pm 8.6	100	0.3 \pm 0.07	100	0.5 \pm 0.17	100	0.6 \pm 0.21	100	44 \pm 9	100	16 \pm 2
6° Head-down subjects															
Control-day 7															
30	139 \pm 4	9	8 \pm 1.8	24	4 \pm 0.7	18	0.4 \pm 0.10	32	0.7 \pm 0.33	30	1 \pm 0.13	29	68 \pm 6	23	26 \pm 11
60	293 \pm 34	29	5 \pm 0.7	38	3 \pm 0.2	30	0.2 \pm 0.04	45	0.4 \pm 0.14	48	0.6 \pm 0.13	46	48 \pm 4	40	14 \pm 3
90	343 \pm 23	51	4 \pm 0.5	50	3 \pm 0.2	44	0.1 \pm 0.02	55	0.1 \pm 0.02	52	0.3 \pm 0.03	56	34 \pm 4	51	10 \pm 5
120	344 \pm 19	74	4 \pm 0.8	62	3 \pm 0.2	60	0.2 \pm 0.04	68	0.2 \pm 0.02	61	0.3 \pm 0.02	66	35 \pm 2	63	10 \pm 1
180	269 \pm 28	92	7 \pm 1.7	83	5 \pm 0.4	83	0.3 \pm 0.11	92	0.4 \pm 0.07	78	0.6 \pm 0.09	84	58 \pm 2	83	16 \pm 2
240	122 \pm 36	100	6 \pm 1	100	4 \pm 0.7	100	0.1 \pm 0.03	100	0.5 \pm 0.10	100	0.5 \pm 0.07	100	51 \pm 5	100	11 \pm 1
R + 2															
30	121 \pm 25	8	8 \pm 1.1	22	3 \pm 0.6	19	0.7 \pm 0.10	39	1 \pm 0.28	36	0.9 \pm 0.24	38	83 \pm 10	26	19 \pm 1
60	351 \pm 23	31	5 \pm 0.7	35	2 \pm 0.4	34	0.3 \pm 0.06	55	0.2 \pm 0.09	43	0.3 \pm 0.04	50	53 \pm 6	43	12 \pm 2
90	384 \pm 12	57	5 \pm 1.5	49	2 \pm 0.3	47	0.2 \pm 0.03	64	0.2 \pm 0.06	50	0.2 \pm 0.05	60	36 \pm 1	54	11 \pm 2
120	295 \pm 53	76	4 \pm 0.02	59	2 \pm 0.4	61	0.1 \pm 0.03	72	0.3 \pm 0.07	61	0.2 \pm 0.04	68	35 \pm 1	65	9 \pm 1
180	274 \pm 96	95	7 \pm 1	79	3 \pm 0.7	81	0.2 \pm 0.04	86	0.4 \pm 0.06	75	0.3 \pm 0.06	82	52 \pm 7	82	14 \pm 2
240	83 \pm 11	100	8 \pm 1.6	100	3 \pm 0.5	100	0.2 \pm 0.05	100	0.7 \pm 0.15	100	0.4 \pm 0.07	100	58 \pm 3	100	15 \pm 2

TABLE 38.— BLOOD RESULTS—WATER LOAD TEST: U.S. STUDY

Subjects	Hb g/dl	Osmo, mOsm	Na, mEq/l	K, mEq/l	Aldo, pg/dl	ADH, μU/ml
0°						
Control day 7						
Pretest	14.5 ±0.2	288 ±2	140 ±0.4	3.9 ±0.1	282 ±13	1.21 ±0.21
90 min	14.7 ±0.3	283 ±2	137 ±1 ^a	4.1 ±0.2 ^a	225 ±15 ^a	0.81 ±19
Recovery day 2						
Pretest	14.1 ±0.1	286 ±2	139 ±0.5	3.9 ±0.1	366 ±17	0.98 ±0.34
90 min	13.7 ±0.2	278 ±2	136 ±1 ^a	4.1 ±0.2	226 ±9 ^a	0.28 ±0.07
6°						
Control day 7						
Pretest	14.9 ±0.2	287 ±1	138 ±1	3.9 ±0.2	298 ±26	0.90 ±0.22
90 min	14.9 ±0.3	281 ±1 ^a	137 ±0.2	4.2 ±0.1 ^a	214 ±8 ^a	0.52 ±0.20
Recovery day 2						
Pretest	14.4 ±1	283 ±1	137 ±1	3.9 ±0.1	294 ±20	0.74 ±0.24
90 min	14.3 ±1 ^a	284 ±2	137 ±1	4 ±0.2	181 ±4 ^a	0.23 ±0.05

Note: 90 min – 90 min after loading; HB – hemoglobin; Osmo – osmolarity; Na – sodium; K – potassium; Aldo – aldosterone; ADH – antidiuretic hormone.

^ap < 0.05 compared to control period.

U.S.S.R. Study

During the control period and during recovery, fasting venous samples (50 ml) were taken at 0730, with all subjects supine for 2 hr before sampling. Acid-base balance was determined from blood samples taken simultaneously by index-finger prick. Samples were taken on days 6, 12, and 14 of the control period; on days 2, 4, and 7 of bed rest; and on days 2 and 7 of recovery. Serum and plasma were separated from red cells by centrifugation at 4°C for 20 min at 3,000 rpm.

Urine was collected daily from all subjects throughout the study. Samples were maintained separately and refrigerated (4°C). Total individual daily collections were measured for volume, and urine designated for electrolyte analysis was acidified with nitric acid (0.25 ml concentrated acid per 12 ml urine).

Blood serum enzyme activity was analyzed using spectrophotometry and colorimetry (Boehringer Mann-

heim (GmbH)). Enzyme activity analysis included glutamate dehydrogenase (GDH), sorbitol dehydrogenase (SDH), gamma-glutamyl transferase (γ-GT), leucine arylamidase (LAB), nonspecific cholinesterase (ChE), alkaline phosphatase (LDH), malate dehydrogenase (MDH), isocitrate dehydrogenase (ICDH), creatine phosphokinase (CPK), alanine aminotransferase (ALT), and aspartate aminotransferase (AAT). The LDH and MDH isoenzymes were separated by polyacrylamide gel electrophoresis followed by densitometry, with the activity of each fraction expressed as a percentage of total enzyme activity. Pancreatic carbohydrase-amylase activity in blood and urine was determined by the procedure of Smith and Roe (ref. 52) as modified by Ryzhova (ref. 53); pepsinogen activity in urine was analyzed by an absorption colorimetric method (ref. 54). Equivalent serum and 24-hr urine results to that reported for U.S. subjects are given in tables 40 and 41.

TABLE 39.—ROUTINE HEMATOLOGY: U.S. STUDY

Subjects		RBC, 10 ¹² /l	Hb, g/dl	MCV, ft	MCH, pg	MCHC, g/dl	Retic, %	Retic No. 10 ⁹ /l	RPI	Hct, l/l
Horizontal	Pre \bar{x} \pm SE	4.60 \pm 0.07	14.1 \pm 0.11	90 \pm 1.5	31 \pm 0.7	34 \pm 0.2	0.6 \pm 0.02	27.5 \pm 1.2	0.6 \pm 0.02	0.41 \pm 0.00
In Bed	Day 2 \pm SE	4.09 \pm 0.14 ^a	14.9 \pm 0.08 ^a	102 \pm 3 ^a	37 \pm 1.2 ^a	36 \pm 0.1 ^a	0.5 \pm 0.04	20.2 \pm 1.3 ^a	0.5 \pm 0.03 ^a	0.42 \pm 0.01
	Day 4 \pm SE	4.36 \pm 0.33	15.6 \pm 0.21 ^a	80 \pm 3 ^a	36 \pm 1.1 ^a	36 \pm 0.3 ^a	0.6 \pm 0.02	24.2 \pm 1.3	0.6 \pm 0.07	0.43 \pm 0.01 ^a
	Day 7 \pm SE	4.77 \pm 0.20	14.9 \pm 0.30 ^a	82 \pm 3.1	31 \pm 1.2	36 \pm 0.7	0.6 \pm 0.06	28.5 \pm 3.5	0.6 \pm 0.05	0.42 \pm 0.02
Recovery	Day 2 \pm SE	4.59 \pm 0.07	14.1 \pm 0.20	86 \pm 3.3	31 \pm 0.6	33 \pm 0.6	0.6 \pm 0.08	25.5 \pm 4	0.6 \pm 0.07	0.40 \pm 0.01 ^a
	Day 7 \pm SE	4.51 \pm 0.05	14.3 \pm 0.13	87 \pm 0.8	31 \pm 0.4	34 \pm 0.7	0.7 \pm 0.12	33.8 \pm 7.8	0.8 \pm 0.13	0.39 \pm 0.02 ^a
6° Head-Down	Pre \bar{x} \pm SE	4.67 \pm 0.07	14.1 \pm 0.09	89 \pm 1.2	30 \pm 0.5	34 \pm 0.1	0.5 \pm 0.02	25.7 \pm 0.9	0.6 \pm 0.03	0.42 \pm 0.00
In Bed	Day 2 \pm SE	4.33 \pm 0.07 ^a	14.6 \pm 0.14 ^a	97 \pm 2.3 ^a	33 \pm 0.7 ^a	35 \pm 0.3 ^a	0.5 \pm 0.05	23.4 \pm 2.2	0.5 \pm 0.04	0.42 \pm 0.01
	Day 4 \pm SE	4.26 \pm 0.25	15.1 \pm 0.13 ^a	103 \pm 4.9 ^a	36 \pm 1.6 ^a	35 \pm 0.3 ^a	0.5 \pm 0.07	22.7 \pm 3.8	0.5 \pm 0.05	0.43 \pm 0.01 ^a
	Day 7 \pm SE	4.61 \pm 0.27	15.1 \pm 0.44 ^a	93 \pm 7.4	33 \pm 2.2	36 \pm 0.3 ^a	0.5 \pm 0.05	25.2 \pm 3.9	0.5 \pm 0.05	0.42 \pm 0.02
Recovery	Day 2 \pm SE	4.58 \pm 0.23	13.9 \pm 0.41	86 \pm 2.6	30 \pm 0.7	35 \pm 0.3 ^a	0.7 \pm 0.21	36 \pm 13	0.8 \pm 0.19	0.39 \pm 0.03
	Day 7 \pm SE	4.53 \pm 0.12	13.9 \pm 0.21	85 \pm 1.6	30 \pm 0.5	35 \pm 0.7	0.7 \pm 0.13	32.6 \pm 7	0.8 \pm 0.13	0.39 \pm 0.02 ^a

^ap < 0.05 compared to recovery period.

TABLE 40.- SERUM, BIOCHEMICAL, AND ENDOCRINE DATA: U.S.S.R. STUDY
[Mean \pm SE]

	Mean control period	Bed rest			Recovery	
		Day 2	Day 4	Day 7	Day 2	Day 7
Na, mEq/l						
0°	141 \pm 0.7	139 \pm 1.0	139 \pm 1.2	142 \pm 1.62	138 \pm 0.6	141 \pm 0.8
-6°	141 \pm 0.4	138 \pm 0.9	139 \pm 1.5	141 \pm 1.5 ^a	139 \pm 0.3	140 \pm 1.1
K, mEq/l						
0°	4.2 \pm 0.05	4.14 \pm 0.10	4.08 \pm 0.10	4.00 \pm 0.08	4.00 \pm 1.60	4.10 \pm 0.10
-6°	4.17 \pm 0.06	4.16 \pm 0.07	3.98 \pm 0.10	3.90 \pm 0.08 ^a	4.20 \pm 0.11	4.10 \pm 0.06
Cl, mEq/l						
0°	100 \pm 0.63	99 \pm 1.61	100 \pm 0.70	101 \pm 1.50	98 \pm 0.50	100 \pm 0.98
-6°	100 \pm 0.48	99 \pm 1.22	99 \pm 0.98	101 \pm 1.2	99 \pm 0.70	99 \pm 0.83
mosm, mOsm						
0°	289 \pm 1.3	288 \pm 1.7	290 \pm 2.2	289 \pm 2.50	283 \pm 0.95	285 \pm 1.90
-6°	288 \pm 1.3	285 \pm 1.62	287 \pm 1.78	288 \pm 2.7	285 \pm 3.6	286 \pm 1.41
Ca, mEq/l						
0°	4.75 \pm 0.05	4.75 \pm 0.11	4.68 \pm 0.08	4.72 \pm 0.06	--	4.60 \pm 0.05
-6°	4.6 \pm 0.03	4.86 \pm 0.1 ^a	4.83 \pm 0.09	4.7 \pm 0.06	--	4.58 \pm 0.01
Aldo, pg/ml						
0°	102 \pm 17.1	120 \pm 14.4	205 \pm 80.4 ^a	204 \pm 52.7 ^a	144 \pm 31.6	94 \pm 35.5
-6°	115 \pm 4.9	122 \pm 15.3	126 \pm 17.2	169 \pm 15.3	130 \pm 8.6	133 \pm 10.2
Cortisol						
0°	12.8 \pm 0.88	12.3 \pm 2.24	11.2 \pm 1.7	14.4 \pm 2.42	12.6 \pm 2.14	14.2 \pm 2.32
-6°	11.3 \pm 0.78	11.3 \pm 1.29	12.3 \pm 1.54	13 \pm 1.54	12.2 \pm 2.14	13 \pm 1.60
Angio I, ng/ml/hr						
0°	1.11 \pm 0.08	1.08 \pm 0.24	1.65 \pm 0.16	2.22 \pm 0.51	1.10 \pm 0.20	1.06 \pm 0.25
-6°	1.15 \pm 0.09	1.33 \pm 0.17	2.61 \pm 0.40 ^a	3.05 \pm 0.48 ^a	2.75 \pm 0.68 ^a	1.70 \pm 0.33
Epi, pg/ml						
0°	0.92 \pm 0.13	1.11 \pm 0.10	1.08 \pm 0.08	0.98 \pm 0.10	1.30 \pm 0.20	--
-6°	1.06 \pm 0.13	1.37 \pm 0.08 ^a	1.18 \pm 0.08	0.98 \pm 0.11	1.38 \pm 0.15	--
Norepi, pg/ml						
0°	1.39 \pm 0.14	1.42 \pm 0.13	1.07 \pm 0.05 ^a	0.89 \pm 0.07 ^a	2.24 \pm 0.25 ^a	--
-6°	1.49 \pm 0.13	1.59 \pm 0.10	0.75 \pm 0.06 ^a	0.70 \pm 0.04 ^a	2.19 \pm 0.18 ^a	--

TABLE 40.—CONCLUDED

	Mean control period	Bed rest			Recovery	
		Day 2	Day 4	Day 7	Day 2	Day 7
Glucose, mg/dl						
0°	88.2 ±2.7	86.3 ±7.1	62.3 ±3.6 ^a	83.7 ±8.5	95.6 ±8.0	79.4 ±4.6
-6°	83 ±2.6	100 ±5.6 ^a	61.2 ±8.2	73 ±7.6	78.9 ±11.1	97.3 ±5.6
Insulin, µ/U/l						
0°	30.8 ±1.5	33.8 ±0.5	38.8 ±0.7 ^a	31.5 ±3.1	35.1 ±2.4	33.4 ±6.5
-6°	26.5 ±1.3	26.9 ±3.4	35.4 ±3.8	33.6 ±1.8 ^a	30 ±2.4	30 ±3.2
Chol, mg/dl						
0°	240 ±14	259 ±45	205 ±18	189 ±15	231 ±17	202 ±17
-6°	232 ±12	240 ±10	255 ±36	249 ±35	264 ±20	232 ±12
Uric acid, mg/dl						
0°	7.1 ±0.5	7 ±0.9	6.7 ±0.8	7.7 ±0.7	8.2 ±0.5	8.5 ±0.6
-6°	6.8 ±0.5	6.1 ±0.6	6 ±0.7	6.4 ±0.8	7.3 ±0.4	7.7 ±0.4

^ap < 0.05 compared to control period.

Serum levels of glucose, lactate, pyruvate, triglycerides, and total cholesterol were determined by enzymatic methods; levels of total lipids, nonesterified fatty acids, phospholipids, and beta-lipoproteins were determined by colorimetric techniques. Lipoproteins were separated into fractions by paper electrophoresis, and electrophoregrams were also used to determine alpha-lipoprotein, beta-lipoprotein, and lipid residue fractions. Serum total protein and bilirubin levels, as well as serum and urine urea, uric acid, and creatinine, were determined automatically (Technicon Auto Analyzer II). Protein fractions were identified by acetate cellulose electrophoresis (Photovolt system). Acid-base balance variables were determined using the Siggaard-Andersen method (ref. 55). Values did not show significant changes over the course of the study.

Blood and urine measurable substances associated with metabolism (oxidative enzymes) and liver function did not change significantly in the horizontal and head-down subjects either during bed rest or during the recovery period. Several individuals showed variations in blood enzyme activity in the control period. Such changes were usually within normal limits, but increases above what are

considered normal laboratory values for SDH activity occurred for 7 of 10 subjects during this period. In one horizontal subject, baseline levels for cholinesterase (ChE), leucine arylamidase, GDH, and gamma-GT, as well as SDH, were elevated. In one head-down subject, ChE activity was below normal values in all three phases of the study, suggesting altered liver function before he entered the study. Carbohydrate and protein metabolism, as well as iron content, iron-binding capacity, and blood acid-balance parameters, were generally within normal limits in the control period, except for the levels of serum bilirubin, urine and serum creatinine, and urine uric acid, which tended toward the higher limits of normal. During that same phase, the albumin level in blood was at the upper range of the norm, and the serum globulin level and globulin fractions were toward the lower limits. The blood glucose level of the head-down subjects was significantly elevated on day 2 of bed rest and significantly decreased in both groups by the end of bed rest. There were associated changes (rises) in serum insulin levels (see table 40). The head-down group also exhibited a significant increase in triglyceride level during bed rest.

TABLE 41.- 24-HOUR URINE: U.S.S.R. STUDY

	Mean, control period	Bed rest				Recovery		
		Day 1	Day 2	Day 5	Day 7	Day 0	Day 1	Day 3
mOsm								
0°	861 ±16	880 ±58	1154 ± 67 ^a	1035 ±51	954 ±19	835 ±59	810 ±51	974 ±74
-6°	923 ±26	1007 ±57	1178 ±100 ^a	965 ±33	1041 ±98	903 ±87	895 ±39	973 ±101
Na, mEq/TV								
0°	144 ±6	175 ±14	253 ±21 ^a	176 ±7 ^b	144 ±8	105 ±8 ^a	116 ±13	180 ±18
-6°	136 ±4	239 ±20 ^a	231 ±15 ^a	166 ±6 ^a	176 ±13 ^a	108 ±15 ^a	114 ±3 ^a	158 ±25
K, mEq/TV								
0°	53 ±2	41 ±5 ^b	57 ±5	58 ±6	62 ±2 ^a	63 ±6	50 ±5	53 ±3
-6°	50 ±2	49 ±5	61 ±5	57 ±2	56 ±5	53 ±5	46 ±2	47 ±4
Cl, mEq/TV								
0°	125 ±5	153 ±10 ^b	227 ±14 ^a	226 ±30 ^a	167 ±13 ^a	142 ±12 ^a	157 ±12	199 ±18
-6°	140 ±4	200 ±25 ^b	208 ±15 ^a	176 ±8 ^a	206 ±18 ^a	147 ±9	148 ±14	185 ±28
Ca, mg/TV								
0°	9.9 ±0.7	8.3 ±1	14.6 ±1.3 ^a	12.5 ±1.3	14.3 ±0.8 ^a	8.9 ±0.3	9.5 ±1	10.7 ±1
-6°	9.5 ±1	10.9 ±2	13.2 ±2.8	12.0 ±2.1	13.8 ±1.7	11.2 ±0.7	18.6 ±5	15.1 ±2.5
Creat., mg/TV								
0°	2.03 ±0.07	1.56 ±0.19	2.26 ±0.34	1.74 ±0.18	2.16 ±0.24	1.66 ±0.15	1.98 ±0.27	2.56 ±0.32
-6°	2.28 ±0.10	2.74 ±0.32	2.40 ±0.11	2.22 ±0.11	2.54 ±0.14	2.24 ±0.17	1.96 ±0.19	2.70 ±0.35
Aldo., µg/TV								
0°	12 ±0.0	10.8 ±2.5	17.4 ±2.9	22.6 ±3.1	28 ±5	27 ±4.8	21.3 ±0.1	5 ±2.3
-6°	11 ±0.0	16.4 ±2.5	21.6 ±1.1	25.2 ±2.7 ^b	21.8 ±1.2	30.2 ±1.9 ^b	27.4 ±2.3 ^b	18.5 ±2.2
Epi (free), µg/TV								
0°	12.3 ±0.55	26 ±1.2 ^b	23.8 ±2.8 ^b	23.8 ±3.6 ^b	17.3 ±3	22.5 ±2.9 ^b	26.6 ±2.4 ^b	17.2 ±1.4
-6°	12.6 ±0.44	25.1 ±33	25.9 ±2.4 ^b	17.7 ±1.6	12.8 ±1.3	15.7 ±1.5	24.7 ±2.9 ^b	19.5 ±2.4
Norepi (free), µg/TV								
0°	29.2 ±0.7	47.3 ±3.4 ^b	37 ±4.6	19.7 ±1.5 ^b	16.9 ±1.4 ^b	29.8 ±3.3	48.2 ±1.9 ^b	41.3 ±3
-6°	30 ±0.8	52.7 ±9.1 ^b	40 ±3	21.2 ±1.7 ^b	18.2 ±2.6 ^b	21.6 ±2.9	47.3 ±2.5 ^b	43.7 ±1.3

^ap < 0.01 compared to control period.^bp < 0.05 compared to control period.

Note: Epi – epinephrine; Norepi – norepinephrine.

Fluid and electrolytes—Fluid intake and content of foods were measured and recorded for each subject. Estimates were based on a summation of water content of beverages in the diet, moisture content of food, and water consumed by the subjects. The subjects in both groups lost weight during the study, the weight of the horizontal subjects dropping by 0.7 kg and the head-down group by 1.7 kg. The principal decrease in body weight occurred during the first 3 days of bed rest. Intake-output balance was determined as the difference of water and electrolyte intake and urine loss (fig. 9). A marked diuresis with bed rest was not present. Because of the marked variation in subject body weights (65-85 kg), fluid intake was normalized to milliliters per kilogram of body weight. The diet and urine were analyzed for the following: electrolytes and minerals, sodium and potassium concentrations (flame photometry), calcium and magnesium (atomic absorption), urine chlorides (titrimetry), urine osmolality (cryoscopy), and urine specific gravity (at 20° with urometer).

Analyses of serum electrolytes indicated no significant changes in ion concentration or in blood osmolality in either subject group during or after bed rest (table 40). Serum potassium did tend to decrease in several subjects on days 4 and 7 of bed rest, but the changes were not significant. Serum aldosterone levels showed a marked increase in horizontal subjects (doubling) and lesser increase in head-down subjects. Serum angiotensin I levels increased in both groups by the end of bed rest, with a much more marked elevation for head-down subjects. Adrenaline levels showed little change over the course of the study, but noradrenaline decreased significantly during bed rest for both groups.

During bed rest, water intake decreased (compared to control), particularly in the horizontal group and increased slightly throughout the recovery period, but did not reach baseline values by the end of the study for either group (see fig. 9).

Intake-output values, converted to kilograms of body weight, did not differ significantly between the two groups during the control period. During bed rest, the horizontal subjects exhibited a significant increase in urine excretion on days 2 and 5, and the head-down subjects varied considerably on all bed-rest days. Urinary fluid loss increased in both groups of subjects on the first 2 days of bed rest, and was particularly noticeable in the horizontal subjects. Slight to significant fluid retention was a feature of the early recovery period (day 0) as has been the case in most previously reported studies. Both groups had fluid balance values close to baseline levels throughout the recovery period.

Values for urine electrolytes, biochemical, and endocrine factors are given in table 41. Renal sodium excretion varied significantly during the control period in both groups, but stabilized before the beginning of bed rest. During bed rest, the horizontal subjects exhibited a significant natiuresis from days 1 to 5, which returned to baseline levels by the end of bed rest. The head-down subjects exhibited a significant ($p < 0.5$) increase in urine sodium excretion throughout the bed-rest period. A significant ($p < 0.05$) difference between the two groups was noted during the first few days of bed rest and was more pronounced in the head-down subjects. On the first day of recovery, both groups exhibited sodium retention. Chloride-excretion responses throughout the study were similar to sodium responses.

Potassium excretion was uniform, with minor individual differences throughout the study, except that the horizontal subjects exhibited a significant elevation at the end of the study.

Renal excretion of calcium did not differ between the two groups during the control period. During bed rest, urine calcium increased significantly in the horizontal group by day 2 and returned to baseline values to a lesser extent in head-down subjects. Values returned to baseline during recovery in horizontal subjects but continued to be elevated in the other group of subjects.

Urine osmolality increased significantly for both groups by day 2 of bed rest.

Changes in renal hemodynamics that occur with exposure to weightlessness and bed rest appear to occur in response to an increase in central blood volume. In addition, observed changes in fluid-electrolyte response during weightlessness are felt to result from suppression of thirst. Findings with bed rest, particularly when in the head-down position, indicate that fluid intake is lowered and could contribute to the observed changes. In the present study, group differences could not be found for many indices, although some shifts in serum electrolyte concentrations and osmotic concentrations were more pronounced in the head-down subjects. Differences between the horizontal and head-down subjects that might have been present were difficult to extract because of the small number of subjects and their individual variations.

Body-fluid compartment changes are given in table 36. Plasma volume and blood volume showed expected decreases during bed rest for the horizontal subjects and returned to, or above, resting levels during recovery. The head-down subjects showed a slight but insignificant increase of blood volume with bed rest. Both groups demonstrated expected changes for extracellular fluid and total body water.

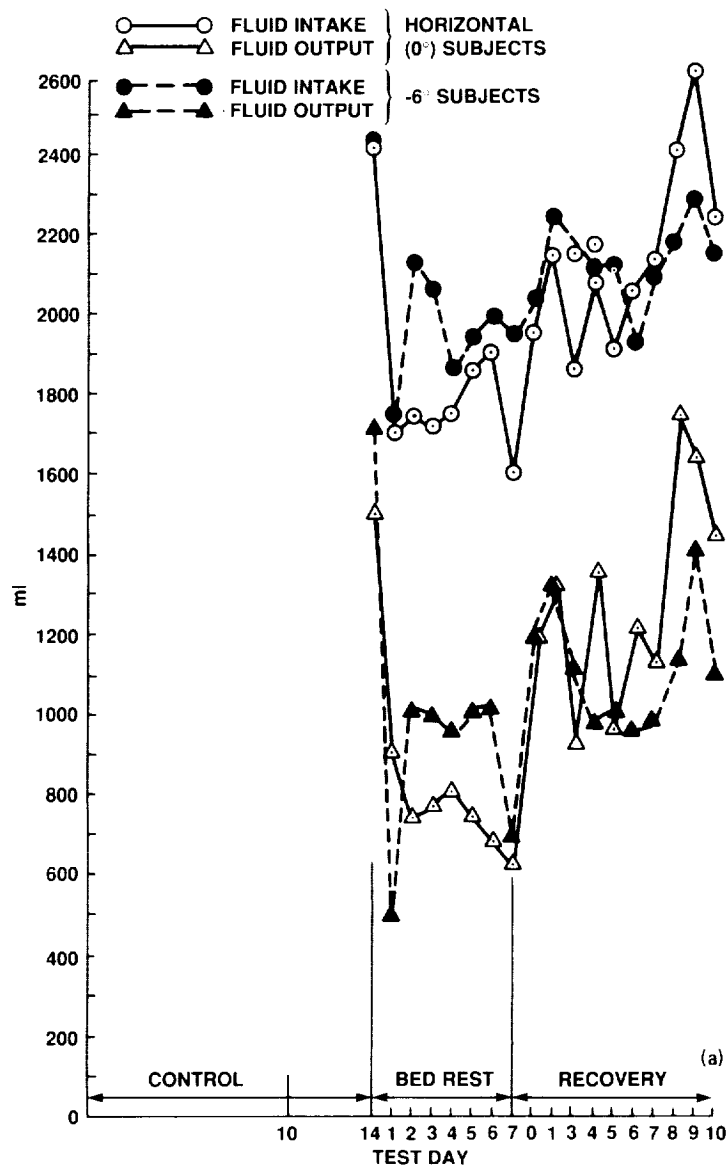


Figure 9.— Mean fluid balance: U.S.S.R. subjects. (a) Fluid intake, fluid output.

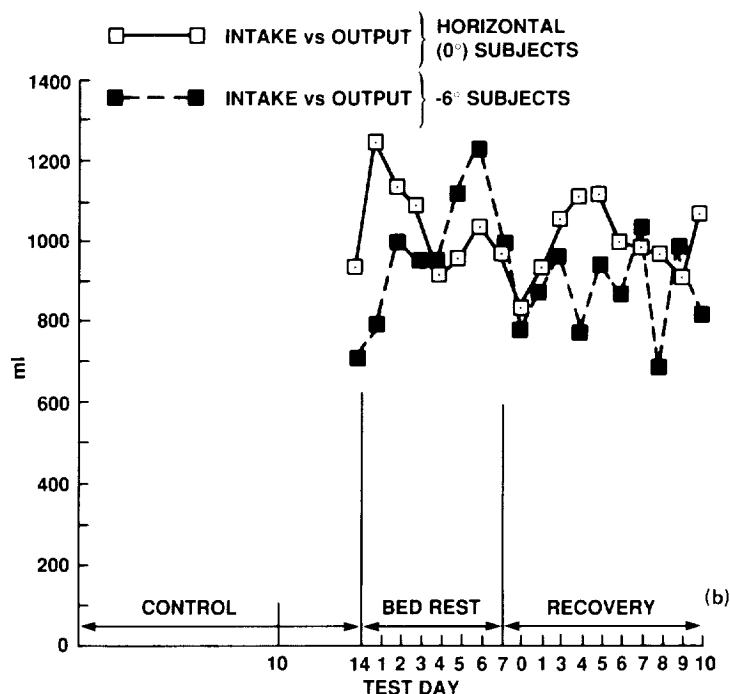


Figure 9.- Concluded. (b) Intake versus output.

Water load test— The water-load test was performed according to procedures described by Noskov et al. (ref. 56). Tests were conducted on the morning of day 9 of the control period and on the second day of recovery, with the subjects in the fasting state and deprived of liquids overnight. After venous blood samples were drawn, the subjects were permitted to urinate and then were weighed and required to drink an amount of distilled water (20 ml per kilogram of body weight). The test required 4 hr, with urine collected every 30 min during the first 3 hr (six urine samples per subject) and a final collection at the end of the 4 hr. The subjects were not permitted to eat, drink, or smoke during the test. They were also kept in the horizontal and head-down positions during testing and permitted to urinate only at times specified by the procedures. Urine collected on the previous night and during the remainder of the test day was also analyzed. Venous blood samples (5 ml) were obtained 90 min before and after water loading.

All blood and urine samples were analyzed for osmolality sodium, potassium, calcium, magnesium, creatinine and 17-HCS after enzymatic hydrolysis using beta-glucuronidase (ref. 57). Data were analyzed using standard concentrations and clearance formulation procedures (refs. 58-60). Urine and plasma results are shown in tables 42 and 43, respectively.

During the control period following water loading, urine fluid loss increased in both groups of subjects, the

greatest excretion rates occurring at 60 to 120 min after loading. Values increased 15 to 20 times baseline rates, reaching 12 and 13 ml/min. As urine volume increased, urine electrolyte concentrations decreased, reaching the lowest level at the peak of diuresis (see table 43). Both subject groups showed a significant decrease in serum sodium concentration and osmolality. However, the two groups did not show significant differences in these regards (see table 43).

Urine osmotic concentration decreased progressively after water loading and reached the minimum level at the peak of diuresis (60 to 120 min); at that point, it was 15 times lower than on the previous night. Osmotically free water clearance increased gradually to a maximum at peak water diuresis, amounting to 10 ml/min in both groups of subjects. The result of this test indicates that excess fluid consumption by normal humans increases body fluid volume and decreases the concentration of osmotically active substances, activating reflex mechanisms that inhibit ADH. An increase in serum osmolality as excess water is eliminated helps to restore serum ADH which, in turn, effects permeability of the distal nephron and collecting ducts for water. Consequently, urine osmolality gradually increases to the end of the test, and finally exceeds serum osmolality. At this point, free water clearance becomes negative.

TABLE 42.— URINE RESULTS, H₂O LOAD TEST: U.S.S.R. STUDY

	Vol., ml	Na, mEq/l	K, mEq/l	Ca, mEq/l	Creat., mg/l
Horizontal -0°					
Control period (day 7)					
At maximum diuresis		9.6 ±0.82	4.90 ±0.27	0.66 ±0.17	0.11 ±0.01
Clearance, ml/min		0.97 ±0.09	15.8 ±0.57	1.92 ±0.55	104 ±8.3
Total excretion, 4 hr	1326 ±135	29 ±2.3	14.0 ±0.5	1.78 ±0.22	376 ±11
Recovery day 2					
At maximum diuresis		9.28 ±1.19 ^a	4.78 ±0.57	0.53 ±0.06	0.14 ±0.01
Clearance, ml/min		0.90 ±0.10	14.7 ±1.52	1.55 ±0.18	133 ±8.3 ^a
Total excretion, 4 hr	1436 ±140	30.2 ±2.9	15.2 ±2.3	1.97 ±0.21	430 ±14
Head-down -6°					
Control period (day 7)					
At maximum diuresis		7.9 ±0.55	4.72 ±0.52	0.48 ±0.04	0.12 ±0.01
Clearance, ml/min		0.75 ±0.04	13.64 ±0.84	1.50 ±0.13	104 ±8.5
Total excretion, 4 hr	1395 ±55	24.4 ±1.4	14.2 ±0.6	1.94 ±0.08	433 ±25
Recovery day 2					
At maximum diuresis		6.7 ±0.88 ^a	3.64 ±0.42	0.50 ±0.08	0.15 ±0.02
Clearance, ml/min		0.68 ±0.05	12.09 ±1.12	1.49 ±0.27	143 ±1.0 ^a
Total excretion, 4 hr	1393 ±179	22.3 ±1.8	12.4 ±0.8	2.14 ±0.33	473 ±65 ^a

^ap < 0.05 compared with control period.

Urine test results (table 42) showed no significant change following bed rest except for creatinine excretion, which was higher ($p < 0.05$) in both groups following loading, and a significant decrease in sodium clearance. These changes correlated with serum sodium decreases and relative stability of other ions 90 min after loading (table 43).

A lack of significant change in renal function with water loading following bed rest was felt to be due to testing on the second day of recovery rather than immediately after the end of bed rest. In previous tests performed at that time, osmoregulatory changes have been observed, including the retention of fluids, electrolytes, and osmotically active substances.

Hematology— Routine hematology during the U.S.S.R. study is shown in table 44. Hemoglobin and hematocrit increased slightly and similarly in both groups during bed rest, as it had in the U.S. study. Following bed

rest, these variables decreased below baseline values. These changes were consistent with known body-fluid volume changes, as shown in table 36. Red cell mass decreased in both subject groups, but did not do so significantly as it had in the U.S. study. Reticulocytes (table 44) decreased in both subject groups during bed rest, but more so in the head-down subjects. Significant increases in platelets occurred for both groups after bed rest. Findings, in general, paralleled U.S. findings.

Endocrinology— Serum and urine samples were used to evaluate sympathoadrenal system status. Blood and urine samples were analyzed for epinephrine, norepinephrine, and dopamine, and for urinary breakdown products (metanephrine, normetanephrine, and vanillyl-mandelic and homovanillic acids). The catecholamine content in blood was measured by fluorescence spectrometry (Hitachi Model MPF-3).

TABLE 43.- SERUM ELECTROLYTE CONCENTRATION AND OSMOTIC CONCENTRATION DURING THE WATER-LOADING TEST: U.S.S.R. STUDY

Constituent		Before bed rest				After bed rest			
		Before loading		After loading		Before loading		After loading	
		0°	-6°	0°	-6°	0°	-6°	0°	-6°
Sodium, mEq/liter	M	143	142	139 ^a	139 ^a	143	143	140	140 ^a
	SD	2.2	1.2	0.92	1.1	2.2	1.4	2.3	1.0
	SE	0.9	0.5	0.4	0.5	1.0	0.6	1.0	0.4
Potassium, mEq/liter	M	4.43	4.18	4.37	4.29	4.35	4.19	4.40	4.34
	SD	0.14	0.21	0.25	0.35	0.18	0.28	0.09	0.30
	SE	0.06	0.09	0.11	0.15	0.08	0.12	0.04	0.13
Calcium, mEq/liter	M	4.67	4.61	4.68	4.64	4.59	4.83	4.63	4.79
	SD	0.21	0.14	0.16	0.09	0.16	0.21	0.18	0.21
	E	0.09	0.06	0.07	0.04	0.07	0.09	0.08	0.09
Magnesium, mEq/liter	M	2.11	1.97	2.12	2.02	2.20	2.09	2.14	2.10
	SD	0.14	0.18	0.14	0.09	0.12	0.07	0.12	0.14
	SE	0.06	0.08	0.06	0.04	0.05	0.03	0.05	0.06
Chlorine, mEq/liter	M	103	102	101	100	100	103	103	99
	SD	3.2	2.8	1.6	1.6	2.8	2.5	1.8	3.0
	SE	1.4	1.2	0.7	0.7	1.2	1.1	0.8	1.3
Osmotic concentration, mOsm/liter	M	291	289	284 ^a	280 ^a	290	289	283 ^a	261 ^a
	SD	4.1	1.4	2.1	3.45	2.5	5.1	2.1	5.1
	SE	1.8	0.6	0.9	1.5	1.1	2.2	0.9	2.2

^ap < 0.05 compared with baseline.

Blood samples were also analyzed for ACTH, cortisol, STH, insulin, glucagon, thyrotropic hormone, thyroxine, tri-iodothyronine, parathyroid hormone, follicle-stimulating hormone, luteinizing hormone, aldosterone, cyclic adenosine monophosphate and cyclic guanosine monophosphate, prostaglandins, pressor and depressor groups, and plasma renin activity. Radioimmunoassay was used to determine hormonal and biologically active compounds in blood samples and aldosterone level in urine. Radioactivity was counted using an automatic gamma-counter (Nuclear Model 1085) and liquid scintillation system (Searle Delta 300).

During the control period serum levels of hormonal and similarly biologically active compounds were generally within normal limits in both groups of subjects (see table 40), although blood insulin level was noticeably higher for horizontal subjects. Furthermore, in this phase,

the head-down subjects exhibited higher levels of ACTH, LH, T₄, TSH, and PTH and significantly lower levels of cAMP/cGMP ratio than did the horizontal subjects. It was felt that these group differences probably resulted from individual responses to the relative restriction of activity during the pre-bed rest ambulatory period.

Renin-angiotensin-aldosterone indices also tended to decrease over the control period. During bed rest, however, these factors tended to increase in both subject groups. In the horizontal group, angiotensin I increase was not significant by the end of bed rest; however, it was significant in the head-down group (p < 0.05) on days 4 and 7 of bed rest. Urinary aldosterone increased gradually during bed rest. This was associated with an increase in serum levels for both groups which was greater for the horizontal subjects (table 40).

TABLE 44.— ROUTINE HEMATOLOGY: U.S.S.R. STUDY

Subjects		RBC, 10 ¹² /liter	HB, g/dl	MCV, fl	MCH, pg	MCHC, g/dl	Retic. No., 10 ⁹ /liter	Hct, liter/liter
Horizontal	Pre $\bar{x} \pm SE$	4.59 ± 0.07	14.5 ± 0.14	91.5 ± 1.2	31.7 ± 0.5	33.9 ± 0.5	6.9 ± 0.5	42.5 ± 0.5
Bed rest	Day 2 $\pm SE$	4.34 $\pm 0.11^a$	14.7 ± 0.22	97.5 $\pm 2.5^a$	34.2 ± 0.1	35.0 ± 0.4	5.2 $\pm 0.6^a$	42.2 ± 0.6
	Day 4 $\pm SE$	4.53 ± 0.12	15.5 $\pm 0.23^a$	96.3 ± 1.8	34.5 ± 0.9	35.5 $\pm 0.4^a$	6.7 ± 0.8	44.0 $\pm 1.1^a$
	Day 7 $\pm SE$	4.71 ± 0.10	15.1 $\pm 0.19^a$	90.7 ± 1.6	32.1 ± 0.7	35.3 $\pm 0.4^a$	6.0 ± 0.9	43.6 ± 0.6
Recovery	Day 2 $\pm SE$	4.29 $\pm 0.13^a$	13.9 $\pm 0.26^a$	93.3 ± 2.7	32.4 ± 0.9	34.7 ± 0.6	7.3 ± 1.0	39.8 ± 0.7
	Day 4 $\pm SE$	4.24 $\pm 0.13^a$	13.8 $\pm 0.23^a$	95.7 $\pm 3.2^a$	32.7 ± 0.9	34.5 ± 0.8	9.3 $\pm 1.6^a$	41.2 ± 0.9
6° Head-down	Pre $\bar{x} \pm SE$	4.65 ± 0.06	14.6 ± 0.17	91.8 ± 1.1	31.4 ± 0.4	34.1 ± 0.3	6.0 ± 0.4	43.6 ± 0.4
Bed rest	Day 2 $\pm SE$	4.51 ± 0.08	14.8 ± 0.15	95.1 ± 0.5	32.7 $\pm 0.4^a$	34.7 ± 0.4	5.0 $\pm 0.6^a$	43.4 ± 0.8
	Day 4 $\pm SE$	4.52 ± 0.16	15.5 $\pm 0.53^a$	98.1 $\pm 2.9^a$	34.5 $\pm 0.9^a$	35.4 $\pm 0.5^a$	6.3 ± 1.0	45.0 ± 0.8
	Day 7 $\pm SE$	4.75 ± 0.13	15.5 $\pm 0.25^a$	94.5 $\pm 3.3^a$	32.8 $\pm 1.0^a$	34.8 $\pm 0.5^a$	6.8 ± 0.9	46.8 ± 0.9
Recovery	Day 2 $\pm SE$	4.51 ± 0.12	14.2 ± 0.26	91.3 ± 2.2	31.6 $\pm 0.7^a$	34.6 ± 0.3	8.1 $\pm 1.2^a$	41.6 $\pm 0.6^a$
	Day 4 $\pm SE$	4.44 $\pm 0.10^a$	13.9 ± 0.29	92.7 ± 2.5	31.2 ± 0.7	34.0 ± 0.8	10.0 $\pm 1.6^a$	42.4 ± 0.5

^ap < 0.05 compared with control period.

ACTH tended to increase in the horizontal subjects on days 2 and 7 of bed rest and on both test days during recovery, whereas it did not vary significantly from baseline values in the head-down group. Excretion of 17-KS in the control period was significantly higher in the head-down subjects than in the horizontal group, but no significant differences were noted between the two groups during bed rest or recovery. The blood luteinizing hormone level tended to decrease in the horizontal subjects again on days 2 and 7 of bed rest and decreased in the head-down subjects on days 2 and 4 of bed rest. Parathyroid hormone (PTH) decreased gradually throughout bed rest for both groups. PTH remained depressed in the horizontal group throughout the recovery period, while it increased above baseline values in the head-down subjects.

Blood insulin levels were significantly higher in both groups on day 4 of bed rest and continued to be higher on day 7 in the head-down group (see table 40). Glucagon level in the horizontal subjects was 40% higher than baseline, but the head-down subjects showed no change. Although no changes in blood insulin levels were noted in either group during the recovery period, glucagon was significantly decreased in the horizontal group on day 2 of recovery and was still lower than baseline values on

day 7. Conversely, the head-down subjects showed no difference.

The cGMP level in the horizontal subjects on days 2 and 7 of bed rest was significantly elevated from baseline values, but showed no significant change in the head-down subjects. The cAMP concentration and the cAMP/cGMP ratio did not show significant differences with bed rest. There were no changes in either group that were indicative of functional changes in TSH or thyroid.

Catecholamines— During the control-period studies, plasma catecholamine (CA) levels were found to be variable. Although CA content was within normal limits on days 3 and 14 of the control period, it was significantly elevated in both groups on day 9.

During bed rest, the horizontal subjects exhibited significant decreases in serum norepinephrine content on days 4 and 7 and in dopamine on day 7, but there was no noticeable change in epinephrine during the bed-rest period. In the head-down group, norepinephrine and dopamine were significantly reduced on days 2 and 7 of bed rest, and epinephrine was significantly elevated only on day 2. However, there was a significant increase in the epinephrine/norepinephrine ratio in both groups throughout bed rest. On the second day of recovery, norepinephrine content rose above baseline values in both groups. Epinephrine also tended to increase in both

groups on day 2 of recovery. Thus, bed rest was characterized by decreased serum catecholamines in both subject groups, the most pronounced changes occurring in the head-down group.

Urine tests during the control period indicated that catecholamine excretion in both subject groups was within normal limits (see table 41). During bed rest, epinephrine excretion (both free and bound) in both groups increased significantly above normal. Free norepinephrine excretion was also significantly elevated in both groups on the first day of bed rest and decreased thereafter, falling below baseline values in some cases. Bound norepinephrine also tended to increase in both groups during the first 4 days of bed rest. Excretion of free and conjugated forms of dopamine was noticeably elevated in both groups on the first 2 days of bed rest, but tended to decline at the end of bed rest.

Throughout bed rest, free metanephrine increased in both groups compared to control values, and bound metanephrine increased on days 1 and 2 in the horizontal group and on days 4 through 7 in the head-down subjects. No significant changes were seen in either group in excretion of homovanillic and vanillyl-mandelic acids.

During the first 3 days of recovery, there were documented increases of urinary free epinephrine, dopamine, and norepinephrine in both groups (table 41). The horizontal subjects also showed significant elevations of free metanephrine on day 0 and on days 3 through 6; the head-down subjects exhibited increases in the bound form on recovery days 6 through 9. Excretion of homovanillic and vanillyl-mandelic acids did not change significantly for either group.

In summary, changes in blood and urinary catecholamine concentrations and epinephrine/norepinephrine ratio agreed with findings in previous studies and are consistent with stress imposed by inactivity and confinement and an emotional reaction to bed rest. The observed decrease in blood levels of norepinephrine and its precursors in this study supports the previous posed hypothesis that bed-rest-induced decline is the result of a decrease in afferent sympathetic impulse transmission caused by maintaining the body in a horizontal position (ref. 61). No significant difference in endocrine change was observed between horizontal and head-down groups.

Comparison of U.S. and U.S.S.R. Findings

U.S. and U.S.S.R. investigators obtained slightly different findings in their endocrine and metabolic studies. U.S. findings demonstrated greater and more rapid changes for head-down subjects in the early part of bed rest. On the other hand, the U.S.S.R. investigators found

no significant differences between the subject groups. Of note were slight decreases in serum and urinary excretions of sodium and chloride seen in both U.S. groups; there were no changes in serum and/or increased urinary excretion noted in U.S.S.R. subjects. The latter changes are more in conformance with previous reports of changes occurring during bed rest (refs. 1 and 22). Opposite changes between U.S. and U.S.S.R. subjects were also noted for serum norepinephrine, aldosterone, insulin, and cholesterol, and urinary epinephrine and norepinephrine.

The difference in findings for the U.S. and U.S.S.R. teams remain unexplained, but poses a question about the possible roles of nutritional and dietary differences in the two studies. Nutritional status is known to affect endocrine function (refs. 1 and 62) and may influence other physiological systems. For example, it is known that diets high in the simple carbohydrates, such as sucrose, can markedly increase the level of blood triglycerides. The U.S. diet (see tables 5 and 7), in general, contained 100 kcal more per day than the normal daily intake and 60 kcal more than the U.S.S.R. diet. Simple and complex carbohydrate intake was increased by +16% in the ambulatory periods and by +34% during bed rest. Although there is no recommended daily allowance of carbohydrates, nutritionists have shown that increased carbohydrate intake can induce water retention, alter loss of sodium and other cations, alter breakdown of body protein, and prevent ketosis (ref. 63). An intake of 50 to 100 g/day of digestible carbohydrates (complex) is considered to be sufficient for these purposes (ref. 63). The amount of carbohydrate in the study diets of both countries were substantially greater than average (see tables 7 and 8), and particularly so for the U.S. subjects. In this case, the diet was tailored to Shuttle specifications rather than to the nutritional requirements of the bed-rest subjects, and these subjects were not accustomed to such a high carbohydrate intake in their daily lives.

Lastly, small, but significant, differences were seen in body-fluid volume compartment changes in the U.S. and U.S.S.R. subjects (table 36). Expected plasma and blood volume losses were seen for both groups in the U.S. study; head-down U.S.S.R. subjects showed little or no change. Red cell mass loss was seen by both, but changes were significant for the U.S. subjects and not for the U.S.S.R. subjects. A possible explanation may be slight differences in the methods used by the two teams of investigators.

The differences in the endocrine, hormonal, and metabolic findings between the two studies, together with the differences in diet, suggest that in future bed-rest studies, more attention may have to be given to nutritional inputs.

VI. EXERCISE PHYSIOLOGY

Physical working capacity has been consistently reduced following either bed rest or spaceflight (refs. 1 and 2). The observed decrease in exercise tolerance is related to an increase in submaximal and maximal heart rate, and significant decreases in maximal oxygen uptake ($\text{VO}_2 \text{ max}$), maximal stroke volume, plasma volume and red cell mass, hemoglobin concentrations, and orthostatic tolerance. The mechanisms responsible for decreased exercise tolerance following bed rest appear to result from (1) the decrease in hydrostatic pressure within the cardiovascular system, and (2) lower myocardial and peripheral muscle metabolism stemming from reduced physical exercise, as well as confinement itself. Exposure to weightlessness would be expected to decrease postflight exercise tolerance in space crews because $\text{VO}_2 \text{ max}$ is known to decrease in both the supine and upright positions following bed rest. Returning space crews have consistently shown deteriorations in exercise tolerance, and some have exhibited this problem during flight as well (refs. 64 and 65). The loss of exercise tolerance in space crewmen may result from several factors. The weight loss observed in returning crews could affect the tolerance for physical work, because this loss is accompanied by a negative nitrogen balance (ref. 66). A decrease in calf muscle circumference and decreased strength have been observed, as well as a decreased plasma volume (ref. 67).

With bed rest, decreased exercise tolerance is associated with changes in both central (cardiac) and peripheral (tissue oxygen exchange and utilization) mechanisms. Following bed rest, some heart muscle fibers may atrophy, resulting in reduced cardiac output and stroke volume (ref. 2). Alternatively, cardiac contractility may be affected by decreased venous return resulting from decreased peripheral muscle tone (ref. 67), and decreased plasma volume, (ref. 2). Moreover, decreased red blood cell mass, which has been consistently observed with both bed rest and spaceflight, can contribute to decreased oxygen-carrying capacity of the blood, as well as to decreased venous return.

Horizontal bed rest has been the usual analog for weightlessness, but recent investigators have indicated that head-down bed rest more closely reproduced physiological responses exhibited by space crew members (ref. 8). Because a previous study (ref. 3) had noted that cardiorespiratory changes with exercise stress were very small, both after spaceflight and bed rest, the present study sought to obtain data that could be more accurately compared by

1. Determining the decrease in exercise performance under a uniform static workload for both horizontal and head-down bed rest subjects

2. Determining the orthostatic effects of gravity on exercise performance following bed rest by comparing physiological responses to both supine and upright exercise

3. Comparing physiological changes in exercise performance induced by horizontal and head-down bed rest to determine which position more appropriately simulates weightlessness deconditioning

4. Examining relationships between changes in body composition and responses to exercise following bed rest

5. Determining the extent and timing of recovery of exercise tolerance following bed rest

U.S. Study

The subjects selected for the present study were paired to the degree possible (horizontal and head-down) according to maximal oxygen uptake ($\text{VO}_2 \text{ max}$, ml/kg/min), height, and weight to obtain the most realistic data on exercise performance following bed rest in the two positions (see table 3). Before the control period, all selected subjects were familiarized with exercise on the bicycle ergometer (Collins Electronic Bicycle Ergometer) in both the supine and upright positions. Following this orientation, each subject performed a maximal exercise tolerance test on the bicycle ergometer in the supine position. The test began with 3 min at 40 W (245 kg/min) followed by a progressively increasing load (40 W each 3 min) until exhaustion.

The same test was repeated on days 2 and 13 of the control period; however, on those days the test was followed, after a 5-min rest period, by 5 min of exercise at 700 kg/min (115 W) and a 10-min recovery period, in which the subjects were permitted to rest until heart rate had returned to within 10 beats/min of pre-exercise values. At that point, they performed the exercise test in the upright position on a different bicycle ergometer (Quinton Electronic Ergometer). The two bicycles were calibrated precisely with each other. The supine and upright exercise tests were repeated after bed rest (recovery days 0, 5, 10).

During testing, the subjects were monitored for heart rate, blood pressure, VO_2 , ventilatory volume ($\Delta \dot{V}_E$), and respiratory frequency. Heart rate was continuously measured and recorded from sternal ECG leads. Systolic and diastolic blood pressures were measured during the last 15 sec of each minute by standard sphygmomanometer and stethoscope techniques. The subjects used a respiratory valve (Otis-McKerrow), and the volume of expired gas was measured with a high-velocity, low-resistance meter (Parkinson-Cowan). A potentiometer at the gas meter dial transmitted electrical outputs to a two-channel recorder (Brush) so that ventilatory volume and

respiratory frequency were recorded continuously. The expired gas was continuously extracted by a Dynapump (Scientific Products) from a 5-liter mixing chamber (R-Pel) which was placed between the subject and the gas meter and connected to a 2-liter gas bag (Ohio Medical) attached to a valve (Costill-Wilmore). The composition of the gas was determined by an oxygen analyzer (Applied Electrochemistry S3A) and a CO₂ analyzer (Godart Capnograph). Before each exercise test, the analyzers were calibrated with a standard gas which was analyzed using the Scholander technique. Oxygen consumption (VO₂), carbon dioxide production (VCO₂), and respiratory exchange ratio (RER) were calculated using standard equations (ref. 68). Body weight (± 5 g) was recorded before each exercise test.

Data were analyzed by paired or nonpaired t-test. The paired t-test was used to compare differences between the average control-period values (control days 2 and 13) and recovery values (recovery days 0, 5, and 10). The non-paired t-test was used to compare mean values between the two groups on a particular test day and to compare mean changes from resting to peak exercise between the two groups.

Body weight and composition— Following bed rest, mean body weight had decreased insignificantly ($p < 0.01$) in both the horizontal (-1.5 kg, -2.2%) and head-down (-2.1 kg, -2.9%) groups (see table 24). Of interest were the findings indicating bed-rest-induced losses in lean body mass without change in total body fat content. Body weight and lean body mass remained depressed on recovery days 5 and 10.

Respiratory responses— Mean ventilatory responses (V_E , BTPS, l/min) are shown for the two groups in figure 10. The head-down group consistently had higher values of V_E during supine rest, exercise, and recovery, but both groups showed similar responses when upright. Following bed rest, resting V_E in the upright position in the horizontal group was significantly greater ($p < 0.05$) on recovery days 5 and 10 than during the control period. During supine exercise, this group showed an increase in V_E of 10.1% on recovery day 10 (from 50.3 to 55.4 liters/min; $p < 0.05$), and the head-down group showed a 20.1% increase over control-period values (from 54.2 to 65.1 liters/min; NS). On recovery day 5, V_E during supine exercise was slightly higher than baseline values (NS) in both groups, but was significantly higher in both the horizontal ($+18.9\%$; $p < 0.05$) and head-down ($+15.7\%$; $p < 0.05$) groups on recovery day 10. During upright exercise on recovery day 0, both groups showed increases in V_E (horizontal = $+15.8\%$; $p < 0.01$; head-down = $+13.3\%$; $p < 0.05$). The ventilatory volume (V_E) tended to be higher during supine exercise than upright exercise in both the horizontal (NS) and head-down ($p < 0.05$) groups. Following exercise during the recovery

period, both groups exhibited increases in V_E in both the upright and supine positions, with the horizontal subjects showing a 14.7% ($p < 0.05$) increase in the supine position and 18.0% ($p < 0.05$) increase in the upright position; the head-down subjects showed values of 22.5% ($p < 0.05$) and 10.1% ($p < 0.05$), respectively. These values remained elevated in both groups on recovery days 5 and 10, but no significant differences were found between the two groups.

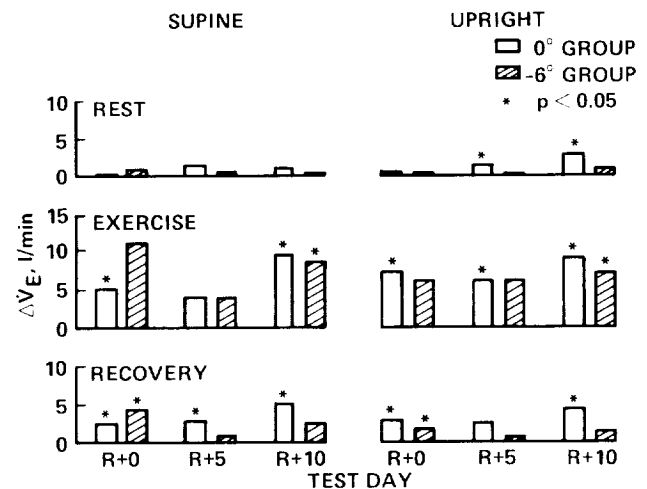


Figure 10.— Difference in mean ventilatory volume (ΔV_E) before and after bed rest: U.S. subjects.

Metabolic responses— There were no significant differences in mean oxygen consumption (VO₂) between the two groups during control testing, although the head-down subjects during this time exhibited consistently higher values during rest, exercise, and recovery in both the supine and upright positions (NS). Differences in the two groups are shown in figure 11. Following bed rest, neither group showed differences in VO₂ during either supine or upright exercise. During supine recovery on day 10, however, the head-down subjects showed a greater VO₂ ($+7.8\%$; $p < 0.05$) than baseline, whereas the horizontal subjects showed no change. During recovery in the upright position, on the other hand, VO₂ was higher than baseline values in both the horizontal ($+8.5\%$; $p < 0.05$) and head-down ($+5.9\%$; $p < 0.05$) subjects. On recovery day 10, both groups showed significantly ($p < 0.05$) higher values of VO₂ during recovery in both the supine and upright positions. Mean resting VO₂ was greater ($p < 0.05$) in both groups in the upright position, but not during exercise and recovery.

Mean carbon dioxide production (VCO₂) measured in liters per minute or in milliliters per kilogram per minute increased significantly ($p < 0.05$) in both groups following bed rest during exercise and recovery in both the supine

and upright positions (fig. 12). The observed values also indicated a significant difference ($p < 0.01$) in RER between the supine and upright positions in the recovery period. During supine exercise, RER increased significantly ($p < 0.05$) in the horizontal group on recovery days 0 and 10 and in the head-down group on day 10.

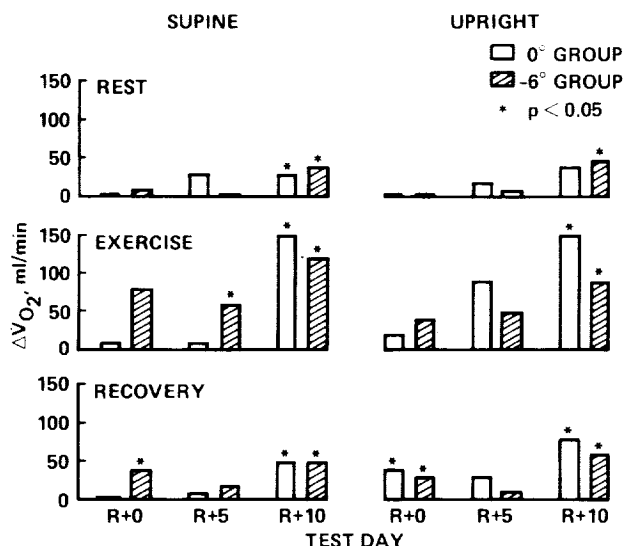


Figure 11.— Difference in mean oxygen uptake ($\Delta\dot{V}O_2$) before and after bed rest: U.S. subjects.

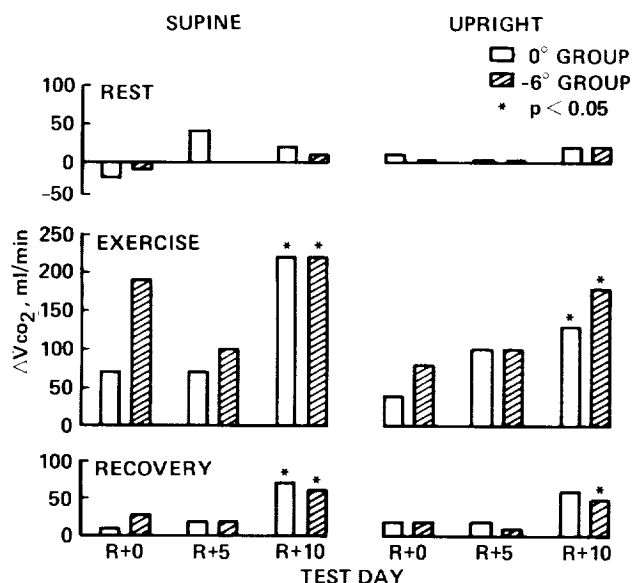


Figure 12.— Difference in mean carbon dioxide production ($\Delta\dot{V}CO_2$) before and after bed rest: U.S. subjects.

Cardiovascular responses— Following bed rest, resting heart rate in both groups was significantly higher ($p < 0.01$) in the upright than in the supine position (fig. 13). During supine exercise, mean HR on the first test after bed rest increased significantly ($p < 0.05$) in both the horizontal (+3.8%) and head-down (+14.3%) subjects. The mean difference in the increase in HR between the two groups (+14 beats/min) was significant ($p < 0.05$). During recovery from supine exercise on recovery day 0, mean HR increased in both the horizontal (+5.5%; $p < 0.05$) and head-down (+17.2%; $p < 0.05$) subjects; the higher HR difference of 11 beats/min for the head-down subjects was significant ($p < 0.05$).

Exercise-induced changes of mean systolic blood pressure were not significant immediately following bed rest or in the subsequent recovery period (fig. 14). Horizontal and head-down subjects during upright testing exhibited a significant ($p < 0.05$) decrease in systolic blood pressure (SBP) during all test periods.

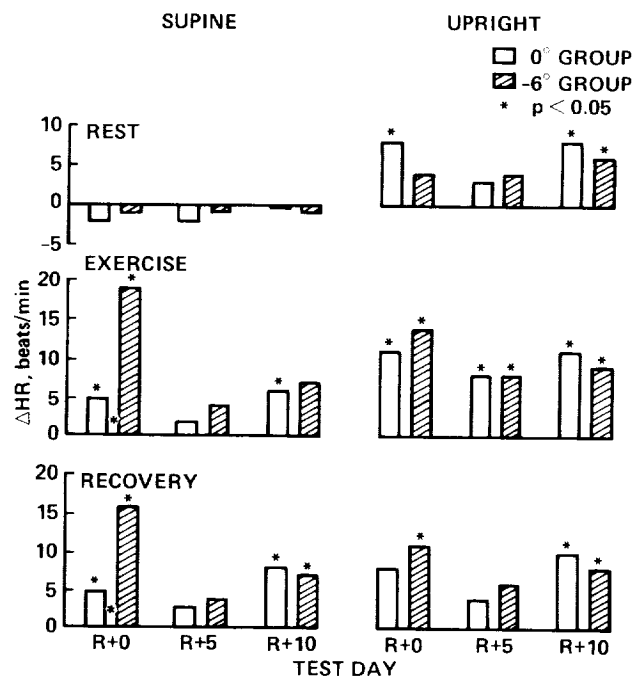


Figure 13.— Difference in mean heart rate (ΔHR) before and after bed rest: U.S. subjects.

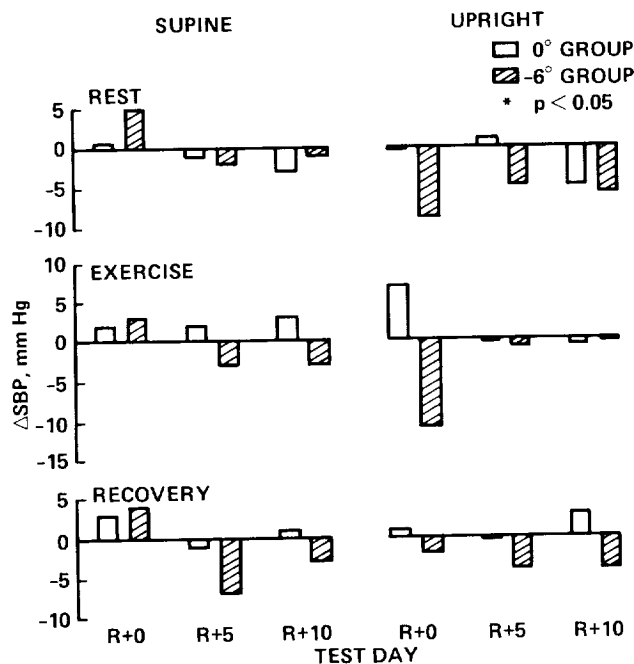


Figure 14.— Difference in mean systolic blood pressure (Δ SBP) before and after bed rest: U.S. subjects.

Resting diastolic blood pressure (DBP) with upright exercise was higher in both groups of subjects following bed rest (fig. 15). In the horizontal subjects, it was significantly higher ($p < 0.01$) than supine values on all test days, reaching 11 mmHg higher than average baseline values ($p < 0.01$) and 10 mmHg higher than head-down values on recovery day 0 ($p < 0.05$). In the head-down subjects, it was slightly higher (NS) on all test days, but showed a significant elevation ($p < 0.01$) on recovery day 5. With supine exercise, the horizontal subjects exhibited an increase in DBP from 96 mmHg (control-period value) to 101 mmHg on recovery day 0, followed by a decrease to 92 mmHg on recovery day 10 ($p < 0.05$). The head-down subjects, on the other hand, showed an increase from 101 mmHg to 107 mmHg following bed rest (recovery day 0, $p < 0.01$) followed by a decrease to 95 mmHg on recovery day 10 ($p < 0.01$). During upright exercise, both groups exhibited significantly lower ($p < 0.05$) DBPs on all test days than during supine exercise. In the horizontal group, DBP during upright exercise on recovery days 0 and 10 was significantly higher ($p < 0.05$) than baseline values. Both groups showed significantly higher ($p < 0.05$) DBP during recovery from upright exercise than during recovery from supine exercise on all test days. On recovery day 0, the horizontal subjects showed an 8% increase (NS), and the head-down group showed a 6% increase ($p < 0.05$).

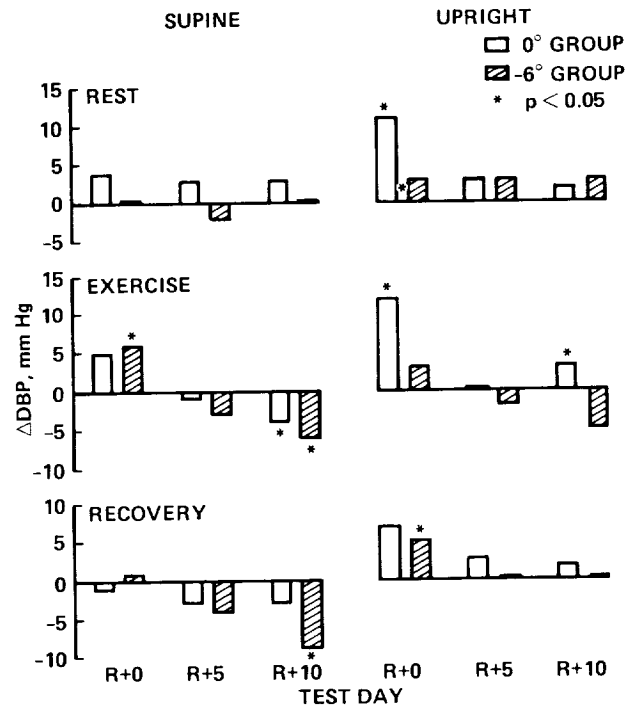


Figure 15.— Difference in mean diastolic blood pressure (Δ DBP) before and after bed rest: U.S. subjects.

Pulse pressure did not change in either group with supine exercise following bed rest for any of the stages of exercise testing (fig. 16). With upright exercise, on the other hand, both groups had significantly lower PP ($p < 0.01$) during rest and recovery on all test days relative to supine values, particularly for the horizontal subjects on recovery days 5 and 10 and for the head-down subjects on control days 2 and 13, and on recovery days 0 and 5. The upright test on recovery day 0 resulted in a significant difference ($p < 0.05$) between the two exercise positions during rest in the horizontal group and during all three stages in the head-down subjects.

The results of the U.S. study indicated the following:

1. Both groups showed a general decrease in exercise tolerance following bed rest.
2. The head-down subjects appeared to lose exercise tolerance following bed rest to a greater degree than the horizontal group, particularly in the supine position.
3. Rest, exercise, and recovery with upright exercise were more stressful in terms of HR and PP responses, suggesting that there is an orthostatic component to the deconditioning effects of bed rest.
4. Despite the return to ambulation, all subjects continued to show decrements in exercise tolerance to the end of the 10-day recovery period, indicating that the deconditioning process was still in effect.

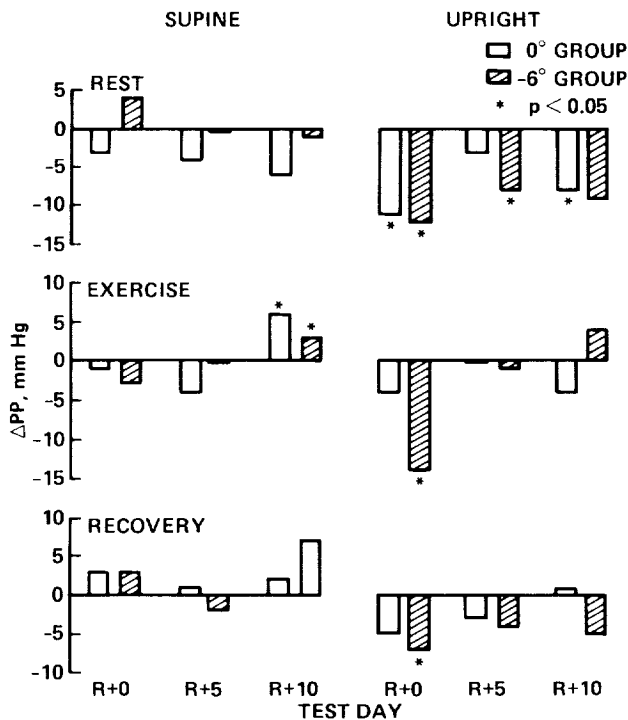


Figure 16.— Difference in mean pulse pressure (ΔPP) before and after bed rest: U.S. subjects.

U.S.S.R. Study

Exercise testing in the U.S.S.R. portion of the study was conducted in both the supine and upright position on a bicycle ergometer (Godart Company) on control days 2 and 13 and on recovery days 0, 5, and 10. Testing was accomplished during the first half of the day, 20 to 25 min after LBNP. If a subject showed poor tolerance for LBNP, the physical load test was delayed for 40 to 45 min. Sensor attachment and equipment calibration were performed during a 10- to 15-min orientation period. Exercise loading was conducted first in the supine position and then in the upright. Both tests followed the same sequence: 7 to 10 min resting, while blood pressure and respiration baselines were recorded; 5 min of bicycle pedaling at a speed of 65 ± 5 rpm (750 kg/min); and 10 min of resting recovery. Oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$) were recorded continuously during all stages of the tests, using an automatic gas analyzer (Junkalor, Spirolit). Maximum ventilatory rates (MVR) were directly measured. Pulse frequency was calculated from the ECG. The percentage content of CO_2 in the

alveolar gas was determined using a capnogram (Godart Capnograph). Gas exchange values, $\dot{V}O_2$ and $\dot{V}CO_2$, were corrected to standard conditions (temperature and barometric pressure).

Changes in exercise tolerance in the U.S.S.R. subjects following bed rest are shown in tables 45 to 50.

Exercise responses in the supine position— In the control period, there were no notable differences in supine exercise tolerance between the two groups except for $\dot{V}O_2$ at rest (table 45). This difference, however, disappeared when $\dot{V}O_2$ was normalized as per kilogram of body weight. During the recovery period following the exercise load, gas exchange (table 46) and respiration (table 47) were essentially the same in both groups. Heart rate (table 48), on the other hand, was higher during recovery in both groups, even after 10 min following test cessation (horizontal = +23.9%; head-down = +13.8%).

Following bed rest (recovery day 0), heart rate at the end of exercise was higher by 5.4% in the horizontal subjects and by 6.4% in the head-down group. By 5 and 10 min into recovery, the head-down subjects showed a return to normal HR, but in the horizontal subjects this variable continued to exceed baseline values by 8.3% at 5 min and 7.5% at 10 min into recovery.

Following bed rest (recovery day 0), systolic and diastolic blood pressure tended to be higher in both groups at rest and during exercise (tables 49 and 50). The systolic pressures were 4 mmHg above control-period values for the horizontal group and 23 mmHg above for the head-down group; diastolic pressures were 9 mmHg and 8 mmHg above, respectively. Evidence of continued deconditioning was seen from HR responses to the recovery-period exercise tests. Heart rate was nearly identical with baseline values in the horizontal subjects, but remained elevated in the head-down subjects on recovery days 5 and 10 (+7.9% and +7.8%, respectively). Gas exchange and respiration values following bed rest were similar to baseline values in both groups.

Exercise responses in the upright positions— During upright exercise in the control period, $\dot{V}O_2$ and $\dot{V}CO_2$ were higher for the head-down subjects than for the horizontal subjects (tables 45 and 46). But when correlated with the subjects' body weights, there was no significant difference. In the head-down subjects during the control period, heart rate was higher and systolic blood pressure lower than in their horizontal counterparts, which differed from the similarity of these findings during supine exercise.

TABLE 45.- O₂ CONSUMPTION (ml/min) DURING EXERCISE: U.S.S.R. STUDY

Group	Indices	Before bed rest				After bed rest, days													
		R	PL	R ₅	R ₁₀	0				5				10					
						R	PL	R ₅	R ₁₀	R	PL	R ₅	R ₁₀	R	PL	R ₅	R ₁₀		
		Exercise while supine																	
		0°	M	275	1702	383	322	291	1691	379	321	311 ^a	1693	354	311	307	1762	393	336
			±SE	12.3	79.1	17.4	8.3	8.4	30.4	18.7	23.2	6.7	51.7	10	14.5	22.9	47	27.3	33
		-6°	M	336 ^b	1769	428	376	344 ^b	1798 ^b	415	303	340	1807	432	376	359 ^b	1821	455	374
			±SE	9.9	60	16.2	18.2	32.8	66	19	19.7	15	97.9	19.5	14.9	14.3	17.4	15.4	20
		Exercise while seated																	
		0°	M	322	1682	360	316	340	1716	396	335	331	1803	377	338	350	1796	405	346
			±SE	12.7	82.3	20.1	17.6	21.3	49.4	33.5	29.4	6.1	43.8	14.6	13.9	23.1	38.9	12.7	24.8
		-6°	M	366	1779	429	3569	365	1756	452	388	369	1818	434	385	383	1827	452	372
			±SE	32.9	88.6	26.5	27	22.9	26.5	20.5	14.5	22.9	109.7	24.1	37.7	24.6	22.1	8.8	22.7

Note: PL = physical load (5 min); R = at rest; R₅ = recovery (5 min); R₁₀ = recovery (10 min).^ap < 0.05 compared to before bed rest.^bp < 0.05 compared to supine.TABLE 46.- EXHALATION OF CO₂ (ml/min) DURING EXERCISE: U.S.S.R. STUDY

Group	Indices	Before bed rest				After bed rest, days													
		R	PL	R ₅	R ₁₀	0				5				10					
						R	PL	R ₅	R ₁₀	R	PL	R ₅	R ₁₀	R	PL	R ₅	R ₁₀		
0° -6°	M ±SE M ±SE	Exercise while supine																	
		245	1714	328	255	260	1792	371	249	289	1766	354	248	277	1834	350	270		
		14.9	88.1	17.8	9.3	14.4	58.4	12.8	33.7	10.9	63.7	9	9.1	17	98.8	16.9	19.5		
		320	1622	377	270	330	1884	411	246	327	1880	421	319	325	1890	421	320		
		26	128	48.3	36.2	27.1	83.4	21.6	13.7	17.9	75.5	43.3	27.1	24.1	101	43.3	17.9		
		Exercise while seated																	
0° -6°	M ±SE M ±SE	252	1507	299	256	257	1591	347	279	244	1667	317	260	282	1623	348	316		
		12.9	77.6	16.7	22.2	11.6	58.9	41.3	31.6	13.8	45.1	10.9	6.9	18.6	42.5	15.5	7.9		
		281	1519	337	274	296	1647	411	320	286	1669	377	313	299	1674	384	305		
		25.5	65.1	40	28.7	25.1	30.9	29.3	10.1	22.8	47.8	37.7	28.9	19.5	23	8.9	11		

Note: PL = physical load (5 min); R = at rest; R₅ = recovery (5 min); R₁₀ = recovery (10 min).

TABLE 47.- MINUTE VOLUME OF RESPIRATION (l/min) DURING EXERCISE: U.S.S.R. STUDY

Group	Indices	Before bed rest				After bed rest, days													
		R	PL	R ₅	R ₁₀	0				5				10					
						R	PL	R ₅	R ₁₀	R	PL	R ₅	R ₁₀	R	PL	R ₅	R ₁₀		
		Exercise while supine																	
		0°	M	9	47	12	11	9	51	13	10	9	49	12	9	10	52	12	10
			±SE	0.6	2.3	0.9	1.4	0.7	1.9	0.8	0.7	0.6	3.3	1	0.8	1.4	2.9	1.2	1.6
		-6°	M	12	50	10	7	11	52	13	11	11	53	15	11	11	55	15	11
			±SE	2.8	2.3	3.2	2.3	1.1	1.1	0.6	0.9	0.9	1.6	0.6	0.9	0.6	1.9	1.5	0.8
		Exercise while seated																	
		0°	M	10	44	10	10	11	50	13	12	11	48	11	10	12	49	12	11
			±SE	0.87	2.9	0.85	1.1	0.8	4	1.3	1	0.6	2.8	0.9	0.7	1.9	2.6	0.8	0.8
		-6°	M	12	47	14	13	13	51	15	13	12	52	14	12	12	50	15	13
			±SE	1.05	2.43	0.9	0.5	1	4.6	1.6	0.8	0.5	2.1	1.3	0.5	0.6	1.6	0.8	0.9

Note: PL = physical load (5 min); R = at rest; R₅ = recovery (5 min); R₁₀ = recovery (10 min).

TABLE 48.- HEART RATE (beats/min) DURING EXERCISE: U.S.S.R. STUDY

Group	Indices	Before bed rest				After bed rest, days													
		R	PL	R ₅	R ₁₀	0				5				10					
						R	PL	R ₅	R ₁₀	R	PL	R ₅	R ₁₀	R	PL	R ₅	R ₁₀		
0° -6°	M ±SE	Exercise while supine																	
		67 4.7	131 4.4	82 6.5	80 7.1	69 4.5	137 8.3	88 8.7	86 8.2	65 4.3	133 5.2	83 8.6	76 4.3	69 3.9	135 4.9	83 6.7	81 6.5		
		72	129	83	82	69	142	84	79	71	136	90	86	73	137	90	89		
		±SE	3.8	4.5	5.2	5.3	5	6.4	5.3	6.1	5.2	6.6	3.4	3.8	4.9	4.9	4.4	3.4	
	0° -6°	M ±SE	Exercise while seated																
			91 ^a	139	94	92	99 ^a	152	113	111	90 ^a	144	96	96	96 ^a	147	96	95	
			±SE	7.9	7.8	9.4	8.5	6.7	8	6.9	7.6	5.4	5.3	6.3	6.9	4	4.8	9.1	7.5
			95	139	98	99	100	154	106	108	96	145	100	100	99	147	103	103	
±SE	2.6	4.3	3.8	4.3	4.3	4.3	6.6	4.9	3.8	7	5.3	5.3	3.5	4.8	3	4.1			

Note: PL = physical load (5 min); R = at rest; R₅ = recovery (5 min); R₁₀ = recovery (10 min).

^ap < 0.05 compared to supine.

TABLE 49.- ARTERIAL SYSTOLIC PRESSURE (mm mercury) DURING EXERCISE: U.S.S.R. STUDY

Group	Indices	Before bed rest				After bed rest, days													
		R	PL	R ₅	R ₁₀	0				5				10					
						R	PL	R ₅	R ₁₀	R	PL	R ₅	R ₁₀	R	PL	R ₅	R ₁₀		
		Exercise while supine																	
		0°	M	136	188	122	115	124 ^a	190	131	118	122 ^a	191	125	118	118 ^a	186	123	112
			±SE	2.9	5.5	4.1	3.5	1	4.8	1.9	1.2	1.9	5.4	2.2	2	2.9	8.4	5.1	3
		-6°	M	126	187	128	121	127	200	131	120	127	193	130	123	129	196	131	122
			±SE	2.5	9.2	5.6	4	6.5	11.6	3.3	4.5	4.6	11.8	5	3.7	4.1	10.5	4.8	5.6
		Exercise while seated																	
		0°	M	113 ^b	164 ^b	120	113	115 ^b	171 ^b	126	118	114	166 ^b	123	118	112	169	122	118
			±SE	4.3	8.7	4.2	4.6	6.2	11.8	4	5.8	6.1	5.9	5.2	4.3	5	9.6	3.7	3.7
		-6°	M	109 ^b	174	107	106	115 ^b	170 ^b	116	115	118 ^b	182	108	109	117	179	116	110
			±SE	4	8.2	6	2.9	2.7	8.2	5.3	3.5	3.1	8.7	4.4	4.8	1.4	10.3	3.7	4.7

Note: PL = physical load (5 min); R = at rest; R₅ = recovery (5 min); R₁₀ = recovery (10 min).

^ap < 0.05 compared to before bed rest.

^bp < 0.05 compared to supine.

TABLE 50.- ARTERIAL DIASTOLIC PRESSURE (mm mercury) DURING EXERCISE: U.S.S.R. STUDY

Group	Indices	Before bed rest				After bed rest, days												
		R	PL	R5	R10	0				5				10				
						R	PL	R5	R10	R	PL	R5	R10	R	PL	R5	R10	
0°	M	Exercise while supine																
		76	92	72	73	83	98	74	82	81	91	73	77	77	99	66	72	
	±SE	1.9	4.2	2.5	2	3.3	5.3	3.3	1.2	2.2	2.4	2.5	1.2	3	1.9	4	3.4	
	-6°	M	78	92	69	74	81	100	75	80	80	92	73	77	80	90	76	82
			±SE	3	3.7	5.1	4	3	3	4.2	3.5	3.5	5.1	4.3	5.8	4.3	5.9	4
	0°	M	Exercise while seated															
82			81	75	72	90 ^a	89	79	82	82	80	73	78	81	81	74	75	
±SE		2.1	3.2	4.2	3.4	2.9	3.7	3.7	3.4	2.7	5.7	4.6	4.4	2.9	6.8	2.9	2.2	
-6°		M	79	84	81	80	87	87	86	87	83	85	76	80	83	84	79	82
	±SE		3.6	6.6	3.7	2.2	4.8	6.2	5.1	3.4	4.6	5.9	5.2	3.5	3.1	7.6	4.3	3.4

Note: PL = physical load (5 min); R = at rest; R₅ = recovery (5 min); R₁₀ = recovery (10 min).

^ap < 0.05 compared to supine.

Significant changes were observed in both groups following bed rest (recovery day 0). At rest before exercise, the horizontal subjects showed an increase in HR of 9.3% and the head-down subjects an increase of 8.5%, relative to control-period values (table 48). At the end of exercise loading, the horizontal subjects showed a 15.6% increase in HR over baseline values, and the head-down group a 12.9% increase. Systolic blood pressure increased slightly in both groups, but diastolic blood pressure showed smaller changes than when supine and increased only slightly from control-period levels (see tables 49 and 50).

During the recovery period following exercise loading, cardiovascular indices in both groups returned to resting levels slowly and were higher by 12.8% in the horizontal group and by 6.9% in the head-down group. On recovery days 5 and 10, HR responses in both groups approached control-period values and normalized more rapidly in the horizontal group. Gas exchange and respiration following bed rest during exercise loading and recovery did not show remarkable changes from control-period values. No significant differences were found between the two groups of subjects.

Thus, during the control period, the two groups of subjects showed resting differences in HR and SBP which disappeared during physical exercise. During exercise, the head-down subjects exhibited higher HRs and a slower return to normal than did the horizontal subjects.

Exercise testing in neither the supine nor upright positions revealed significant differences in responses

between the two groups. Observed cardiovascular changes were more pronounced in the upright than in the supine position, but gas-exchange and respiration indices did not differ significantly between the two. These findings are supported by results with upright exercise testing during Soyuz flights (ref. 69) and Skylab experiments (ref. 70).

Comparison of U.S. and U.S.S.R. Findings

Mean percentage change (%Δ) in \dot{V}_E , $\dot{V}O_2$, and HR during supine exercise and recovery for the horizontal and head-down subjects are compared for the U.S. and U.S.S.R. studies in table 51 and for supine and upright body positions for horizontal subjects in table 52.

The findings during exercise testing, in general were similar for both the U.S. and U.S.S.R. investigations. Both teams of investigators found that exercise in the upright position following bed rest produced greater cardiovascular changes than exercise in the supine position and that head-down subjects showed greater responses and a slower return to normal values. Greater changes were seen for the head-down U.S. subjects for \dot{V}_E and HR. Although absolute values differed between sides, the magnitude of change in going from a lying to sitting position was quite similar. Both concluded that the observed changes were correlated with orthostatic responses occurring with immobilization (and confinement) which tended to be more substantial in the head-down subjects.

TABLE 51.—0° VS -6° SUBMAXIMAL EXERCISE RESPONSE: MEAN PERCENT CHANGES (%Δ) IN \dot{V}_E , $\dot{V}O_2$, AND HR DURING SUPINE EXERCISE AND RECOVERY FOLLOWING 0° AND -6° BED REST

Factor	0° Bed rest				-6° Bed rest			
	Supine exercise		Recovery		Supine exercise		Recovery	
	U.S.	U.S.S.R.	U.S.	U.S.S.R.	U.S.	U.S.S.R.	U.S.	U.S.S.R.
%Δ \dot{V}_E	+10.3 ^a	+8.5 ^a	+15.1 ^a	+8.3 ^a	+24.7 ^{a,b}	+4.0 ^a	+23.9 ^a	+30 ^a
%Δ $\dot{V}O_2$	+0.8	-0.6	0.0	-1	+5.4	-1.6	+10.3 ^{a,b}	-3 ^b
%Δ HR	+3.8 ^a	+4.6 ^a	+5.9 ^a	+6.8 ^a	+13.4 ^{a,b}	+10.1 ^b	+17.6 ^{a,b}	+1.2 ^b

^ap < 0.05 for before vs after bed-rest changes.

^bp < 0.05 vs corresponding 0° bed-rest value.

TABLE 52.— 0° VS -6° SUBMAXIMAL EXERCISE RESPONSE: MEAN PERCENT CHANGES (%Δ) IN VE, VO₂, AND HR DURING EXERCISE AND RECOVERY IN THE SUPINE AND UPRIGHT POSITIONS FOLLOWING 0° BED REST

Factor	Exercise				Recovery			
	Supine		Upright		Supine		Upright	
	U.S.	U.S.S.R.	U.S.	U.S.S.R.	U.S.	U.S.S.R.	U.S.	U.S.S.R.
%Δ VE	+10.3 ^a	+8.5 ^a	+15.6 ^{a,b}	+13.6 ^{a,b}	+15.1 ^a	+8.3 ^a	+17.4 ^a	+30 ^a
%Δ VO ₂	+0.8	-0.6	+1.4	+2.0	0.0	-1	+8.1 ^{a,b}	+10 ^{a,b}
%Δ HR	+3.8 ^a	+4.6 ^a	+8.3 ^{a,b}	+9.4 ^{a,b}	+5.9 ^a	+6.8 ^a	+7.9 ^a	+20.2 ^a

^ap < 0.05 for before vs after bed-rest changes.

^bp < 0.05 vs corresponding supine value.

VII. CONCLUSIONS

The findings of the present study concerning physiological responses to prolonged bed rest in the horizontal and head-down positions were similar to results from previous bed-rest studies and from manned spaceflight experience (refs. 1 and 2). The present study was notable not only because of its comparison of horizontal and head-down bed-rest responses, but also because it was conducted jointly by U.S. and U.S.S.R. investigators.

In both studies, the horizontal and head-down groups showed expected bed-rest-induced differences in biochemical endocrinologic, hematologic, and fluid balance measurements and almost no areas of change specifically attributable to the difference in body position. Findings of particular note were that head-down subjects did not show significantly greater decreases in plasma volume, blood volume, or red cell mass. There also appeared to be no significant differences between responses of the two groups to water loading. Since this test was performed on day 2 of recovery, early recovery-period changes may have been undetected. Significant changes in ECGs and VCGs did not occur in either group. It has been previously hypothesized that the head-down body position during bed rest might produce shifts in heart position within the chest which could be detected and quantified on the VCG tracings. Such evidence did not appear in the present study.

With LBNP and exercise testing following bed rest, the head-down subjects exhibited a slightly greater degree of deconditioning. In this regard, recovery-period exercise testing results for the head-down subjects compared more closely with findings from spaceflights (see table 53).

Exercise testing, both supine and upright, proved to be more sensitive than LBNP in demonstrating recovery-period deconditioning and the patterns of recovery. Despite some indications of a return to baseline values in this group on recovery day 5, the subjects continued to manifest degraded values by recovery day 10. These findings may have been complicated by the somewhat long recovery period (10 days), with the possibility of deconditioning occurring from confinement itself (ref. 2). The horizontal subjects experienced these responses in the recovery period to a greater degree than did the head-down subjects.

Bed rest produced the following significant changes (p < 0.05) during supine exercise and during the 5-min recovery period following exercise:

1. A greater increase in exercise heart rate in the head-down group following bed rest than observed in the horizontal subjects (U.S. = +13.4% versus +3.8%; U.S.S.R. = +10.1% versus 4.6%); the heart rates remained elevated during recovery from exercise testing.

2. Increased ventilatory volume in the head-down group, which also remained elevated during recovery from exercise.

With upright exercise, all subjects exhibited higher heart rates and diastolic blood pressure, but lower ventilatory volume, pulse pressure, systolic blood pressure, CO₂ production, and respiratory exchange ratio than they had during supine exercise. These differences undoubtedly resulted from orthostatic stress and greater blood pooling in the lower extremities. Despite the fact that the head-down group exhibited higher heart rates during supine exercise, the upright exercise values for the two groups were similar. Furthermore, the head-down group showed

TABLE 53.- COMPARATIVE EXERCISE RESPONSES AFTER BED REST AND SPACEFLIGHT

	Δ HR		Δ VO ₂		Δ O ₂ Pulse	
	beats/min	%	ml/min	%	ml/beat	%
0° Bed rest ^a	+5	+3.8	+10	+0.8	-0.4	-3.3
-6° Bed rest ^a	+19	+13.4	+80	+5.4	-1.1	-8.5
Soyuz spaceflight ^b	+13	+11.8	+60	+4.3	-1	-7.7

^aSupine bicycle exercise for 5 min at 700 km/min after 7-day bed rest.

^bIn-flight bicycle exercise for 7 min at 600 km/min after 5-day spaceflight.

lower diastolic blood pressures at rest before upright exercise than the horizontal group, but these rose to horizontal levels during exercise and recovery. Diastolic blood pressures were also significantly lower during upright exercise than supine levels, but were significantly higher at rest and during recovery following exercise. These responses most likely resulted from observed losses in plasma volume.

Water volumetry showed a slight, but highly significant ($p < 0.01$), decrease in lean body mass, with the head-down subjects showing the greatest decrease. Although these changes can be strongly correlated with losses in total body water, they may also explain the greater loss in exercise tolerance seen in the head-down subjects following bed rest by indicating an absolute loss of muscle mass.

LBNP responses from control to peak LBNP (-50 mmHg) were similar in both horizontal and head-down groups before and after bed rest, and the magnitude of change was similar to previous findings reported in the literature (refs. 2 and 71). Responses to LBNP stress followed the same patterns observed with exercise stress. The most significant ($p < 0.05$) changes following bed rest were in heart rate (increased), cardiac output (decreased), stroke volume (decreased), and left ventricular end diastolic volume (decreased). The magnitudes of the changes (derived from data in table 30) are shown in table 54. All parameters showed 20% or better bed rest-induced changes except for SV and CO in U.S. horizontal subjects, which actually got better rather than worsened. The U.S. head-down group maintained greater recovery-period changes, particularly in cardiac output ($p < 0.05$), supporting the conclusion that this group was more severely deconditioned following bed rest than the horizontal subjects.

Leg pooling increased as expected during LBNP, but did not differ significantly between the two subject groups. Pooling studies showed that the pelvic area was the major site for volume shifts during LBNP.

Hemodynamic measurements at rest over the course of the study revealed expected changes in most variables. Differences between observed absolute values for parameters such as end-diastolic volume and arterial blood pressures were most likely the product of dissimilarities in instrumentation.

Analyses of fluid and electrolyte balance also provide evidence that the head-down group may have retained more fluids, which would account for the hemodynamic changes seen in this group between the second and fourth days of bed rest. Between bed-rest days 2 and 6, the head-down group consistently showed positive water balance values that were higher than those for the horizontal subjects. The difference between the two groups was significant ($p < 0.05$) on day 5 of bed rest. On that day, the horizontal subjects exhibited a mild, but significant ($p < 0.01$), diuretic response, whereas the head-down subjects increased their degree of fluid retention. The physiological significance of these differences was corroborated by serum and urine sodium values. Sodium excretion tended to decrease throughout bed rest in both groups and was associated with a significant ($p < 0.05$) decrease in serum sodium in both groups. The fact that the head-down group manifested fluid and hemodynamic changes to a significantly greater degree than did the horizontal subjects suggests that the head-down body position causes significant differences in body-fluid distribution and handling, which is perhaps best explained by an excessive ADH excretion. However, increased urinary and plasma values of ADH were not observed during the present study.

TABLE 54.- PERCENTAGE CHANGE IN PARAMETERS DURING PEAK LBNP: U.S. AND U.S.S.R. STUDIES

Parameter and bed-rest position		Before bed rest		After bed rest	
		U.S.	U.S.S.R.	U.S.	U.S.S.R.
Heart rate	0°	+26	+36	+50	+52
	-6°	+30	+42	+59	+70
Cardiac output	0°	-17	-21	-5	-25
	-6°	-13	-4	-39	-9
Stroke volume	0°	-36	-41	-37	-51
	-6°	-33	-33	-62	-48
Left ventricular end diastolic volume	0°	-34	-38	-39	-42
	-6°	-34	-28	-55	-34

Note: Values represent mean differences between pre-LBNP to peak compared with pre-LBNP levels.

The cause of these latter changes remains unexplained, but there is some indication that differences in nutrition and diet may have played a role. Nutritional status is known to affect endocrine function and may affect other physiological systems. For example, a diet high in simple carbohydrates (e.g., sucrose) can raise blood triglyceride levels. Nutritionists have shown that a diet high in carbohydrates can result in water retention, and can alter loss of sodium and other cations and other physiological responses. Both the U.S.S.R. and U.S. diets were high in carbohydrates, but the U.S. diet significantly so. This diet was designed to simulate that used for

Shuttle astronauts and was not tailored to the nutritional requirements of the bed-rest subjects, most of whom were not accustomed to a high carbohydrate intake in their daily lives. The possibility that dietary differences between the U.S.S.R. and U.S. subjects may have played role in the difference in observed responses suggests that dietary input may require greater attention in future studies.

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16. Abstract <p>An account is given of the results of the first joint U.S./U.S.S.R. bed rest study. The study was accomplished in two parts: a Soviet part (May to June 1979) and an American part (July to August 1979). Both studies were conducted under identical conditions and provided a basis for comparison of physiologic reactions and standardizing procedures and methods. Each experiment consisted of three periods: 14 days of pre-bed rest control, 7 days of bed rest, and a 10- to 14-day recovery period. Ten males participated in each study, with five subjects experiencing horizontal bed rest and five subjects a -6° head-down body position. Biochemical and hormonal measurements were made of blood and urine, with particular attention to electrolyte metabolism and kidney function; cardio-pulmonary changes at rest and exercise; influence of LBNP; and incremental exercise using a bicycle ergometer while supine and sitting. Expected moderate changes were noted to occur for various physiologic parameters. Clinical evidence pointed to the fact that head-down bed rest when compared to horizontal conditions more closely matched the conditions seen after manned spaceflight. For the most part, statistically significant differences between the two body positions were not observed.</p>					
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